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THE AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS

FIRST DAY, JUNE 10, 1943

STONE IN THE LOWER THIRD OF THE URETER

REPORT OF AN INSTANCE OF AN INCARCERATED BASKET

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From the Department of Genito-Urinary Surgery, Indiana University School of Medicine, Indianapolis

Several years ago (November 18, 1941) we had occasion to survey our experience with ureterolithiasis at a meeting of the Section of Genito-Urinary Surgery of the New York Academy of Medicine. During the years 1939 to 1941 inclusive our group (Hamer, Mertz and Wishard) hospitalized 119 private patients with symptoms thought sufficiently suggestive of stone disease by their referring physicians to warrant the attention of a urologist. Nineteen of these (16 per cent) were definitely not ureteral calculi and thirteen (11 per cent) were uncertain, leaving eighty-seven patients (73 per cent) whose admission diagnosis subsequently proved to be correct.

Curiously enough, during the same time interval the University Hospitals had seventeen similar ward patients and the City Hospital had forty. In the latter group seven had stones which did not or would not pass. Four of these seven died. One of the four was the only example we have ever seen of rapidly developing typical uremia in a patient with unilateral ureterolithiasis and a kidney on the other side which, by all demonstrable tests in vivo, appeared to be normal. These two public institutions have well over double the bed capacity of the Methodist Hospital (a private institution), and very active services. Does their lowered incidence of ureterolithiasis indicate that the less well-to-do keep their stones with them always or that calculi and currency are not base enemies?

In retrospect it is easy to classify ureterolithiasis according to what ultimate method is the one of the stone's removal. The accompanying table classifies a 100 chronologically consecutive ureteral

calculi treated in a recent three-year period by our group as private patients.

Patients relieved	75%	
Stone passed spontaneously	17%	
Removed	58%	
Surgically (including 7% instrumental failures)	17%	
Instrumentally	13%	43% of the whole or
Passed after instrumentation	30%	70% of those attempted.
Patients not relieved	25%	
Untreated, not recovered	15%	
Unsuccessful manipulation (7% not counted here because listed above)	10%	
Total unsuccessful manipulations	17%	of the whole,
or of those attempted	30%	
Deaths	0%	

In anticipation, however, such a table is of little aid in selecting the proper method of removal. We have found our own pitfalls in arbitrary overenthusiasm for some particular method. Our belief at present is that each individual is a problem unto himself, rather than that he be arbitrarily treated by a preselected method because the stone is of a given size, shape, location, etc. There are too many variable factors constantly present to form a simple equation to fit every stone in the lower third of the ureter.

When the surgeon is confronted with such a problem there are three courses open to follow. *First*, the course of spontaneous passage, or that of the non-interventionist. If the duration of the illness is short and excretory pyelography shows no serious dilation above, if no serious sepsis is at hand, if the stone is not too large, if there is evidence of downward progress by repeated visualization and if there is no evidence of abnormal ureteral obstruction below the stone, it would be agreed that such a course would be tenable—at least until a change in one of these factors indicates the need of more radical measures. Pregnancy (at least its last trimester), or systemic contraindications to operation, might also put certain patients in this category which would otherwise be better considered elsewhere.

Figure 1 illustrates a typical instance of a stone passing only with observatory films to mark the progress of a small stone which, as will be seen in the last x-ray, delivered itself.

Figure 2 shows an unusually large stone which likewise delivered itself, a catheter being passed to the stone every fifth day to verify its progress. The pyelogram made 1 week after the stone delivered itself shows the pelvis and ureter almost returned to normal.

The *second course* is that of endoscopic instrumentation or manipulation, including everything from a simple ureteral catheter to calculus retrievers of varying degrees of complexity. While the literature might lead one to think that the indications are almost without limit, our own experiences have not all been tranquil even

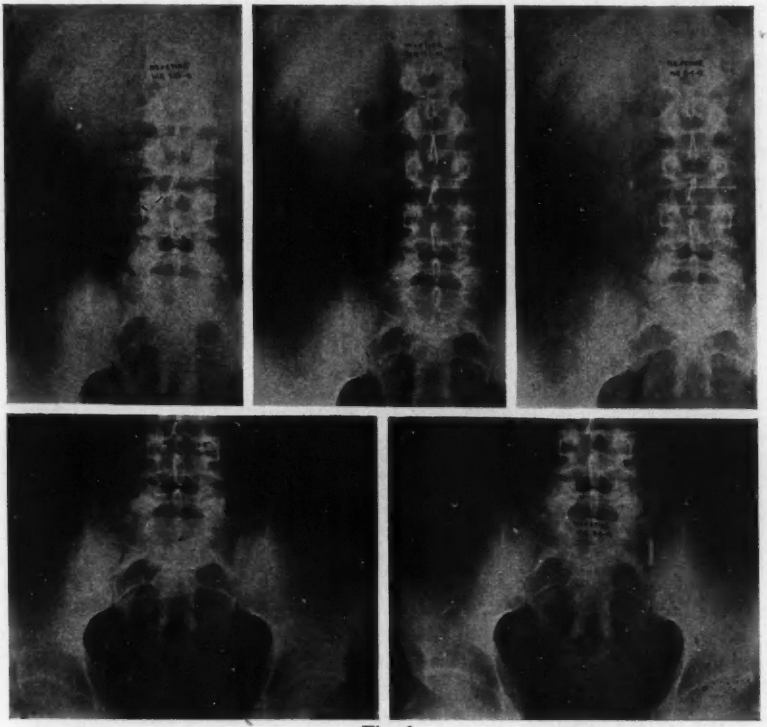

Fig. 1

though we do not tackle whales. We know of no certain way of determining whether or not a given stone is applicable to this method, but we do believe that the selection should come from Group 1, where there has been no progress and no disproportion of size of stone and ureter. We have never had any serious complications from the use of ureteral catheters, single or multiple, but can conceive of much possibility of damage from these barbarous domestic

catheters which filled the interim between the cessation of Eynard's and the development of the excellent present-day pliable domestic catheter. With the retriever, we have had our glittering successes and with the same instrument we know of no method of intensifying and augmenting one's personal anxiety more than between the minute that the stone is grasped and the instrument delivered. At

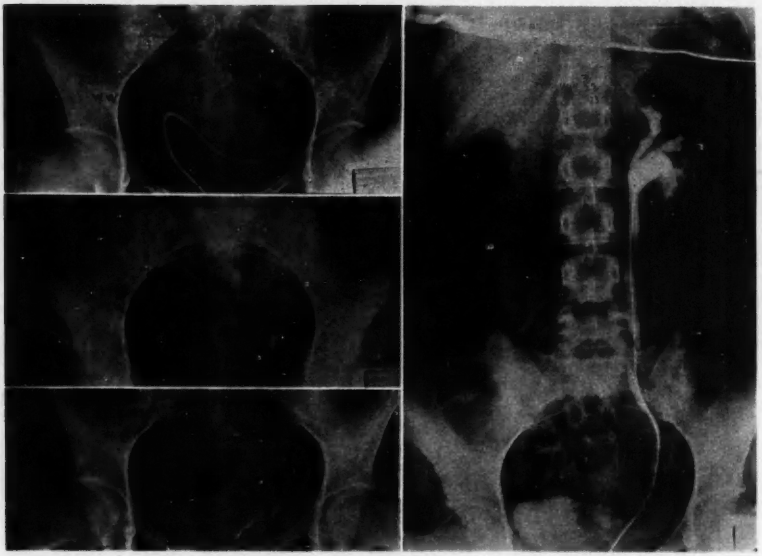

Fig. 2

least twice in our experience this delivery has had to be accomplished above. For ourselves we set down the following arbitrary prerequisites for our future use of baskets: *First,* we must demonstrate to our satisfaction that the stone is making no headway. *Second,* we must prepare the way by the use of indwelling ureteral catheters before attempting extraction. *Third,* the patient must be under a spinal anesthesia. We do not mean to imply that these prerequisites guarantee success but we do believe that they will minimize failure and avoid serious complications. And *fourth,* ureteral catheter drainage must be maintained for several days after extraction until the chart is flat, the urine grossly clear and the roentgenogram free from shadow.

Figure 3 illustrates a successful delivery of stone with basket requiring twenty-four-hour rubber band traction which finally catapulted the basket and stone over the foot of the bed. Predelivery and postdelivery pyelograms are shown.

Our most common (but not most serious) untoward event connected with manipulation is failure. If one had definite data which

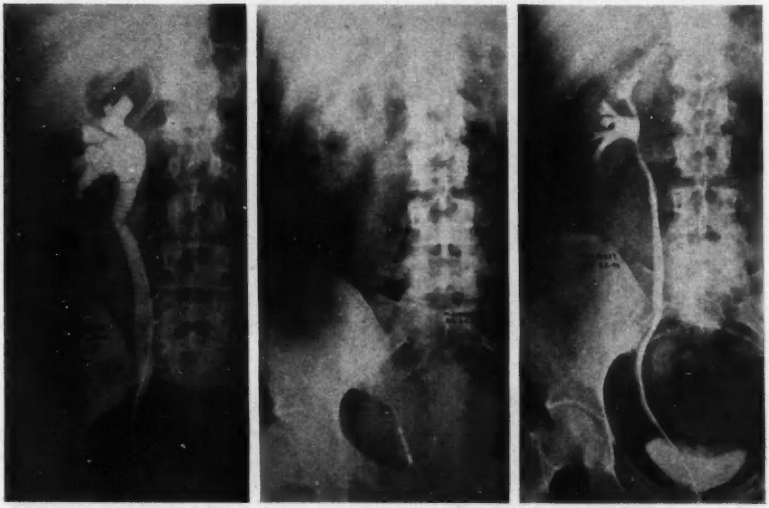

Fig. 3

would enable him to select the route of removal with the certainty that it was the measure which would yield success, these would be of great practical value. Unsuccessful manipulation may not only fail to get the stone but may throw the patient into a septic course which will cause much trouble. Next to failure is alteration of the position of the stone (not necessarily in a favorable direction) or, as we recently saw, rotation of the stone's axis into the transverse diameter with inability to re-introduce ureteral drainage. We have recently experienced such a disaster which was solved only after a perirenal abscess had developed and was drained.

Incarceration of the dislodger is the most serious complication we have had. Breakage or fracture of the instrument would be in the

same category. Discussion of this follows later. Post-instrumental stricture or chronic pain without anatomic abnormalities is also possible.

The *third course* is that of open operation, and is applicable to failure with Courses 1 and 2 as well as to stones obviously too large

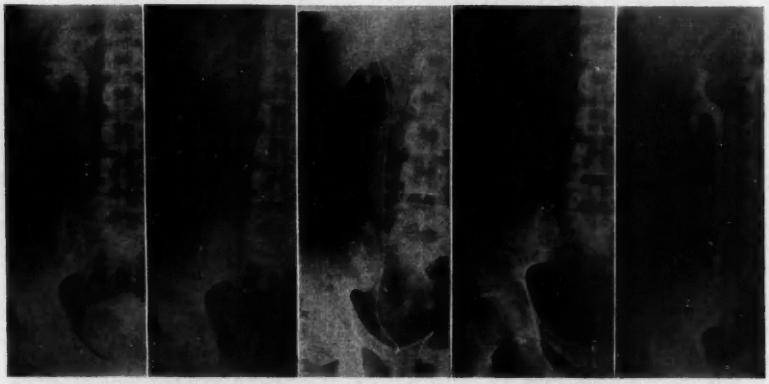

Fig. 4

Fig. 5

to engage in an extractor or to pass spontaneously. We suspect it should be employed more often though Figure 2 shows an instance of a stone which passed spontaneously when our prediction was ureterolithotomy. Course 3 should also be adopted before Courses 1 and 2 have been too long employed to the patient's detriment.

Figure 4 illustrates a point at question. The patient was seen by us a year after he was known to have a stone in the lower right ureter. The first two roentgenograms indicated progress. There was then a quiescent period so that we passed a catheter preparatory to dilation of the ureter (third picture, Fig. 4). The stone here

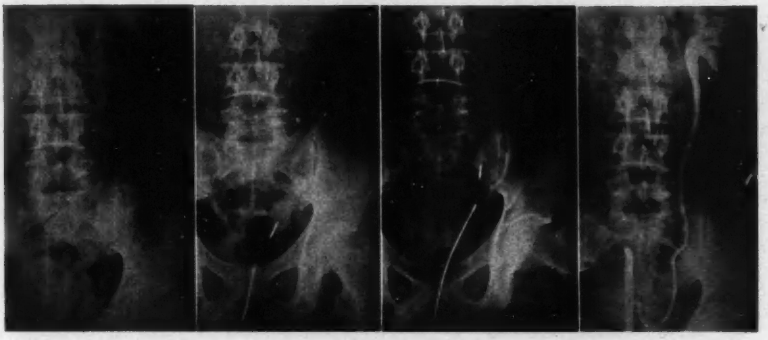

Fig. 6

had moved up to the level of L-4. The catheter slipped out after the stone had come down to the sacral level (fourth picture, Fig. 4). After a short but violent febrile reaction further dillydallying was vetoed and the stone was removed surgically. The last film in Figure 4 (postoperative) shows complete resolution of the preoperative hydronephrosis.

Figure 5 illustrates discouragement in spite of both instrumental and operative methods. The patient was a bad operative risk because of obesity. After adequate dilatation (April 12, 1943) of the ureter a long, narrow stone in the lower third of the ureter failed to pass. Open operation was then performed through a right Gibson incision. Because of extreme obesity incision of the ureter over the stone was difficult so the ureter was opened higher and the stone removed with the Randall forceps. It still being impossible to pass a catheter into the bladder from above, therefore, from below a simultaneous attempt was made cystoscopically to introduce a catheter upward. This was unsuccessful. The operation had to be discontinued because of the patient's condition. Postoperatively (April 26, 1943, Fig. 5) an x-ray showed a hitherto unrecognized

second stone which had passed into the bladder from the right ureter. This was removed with Young's rongeur and a final examination (May 3, 1943, Fig. 5) showed the right ureter patent and free of stones and a normal left pyelogram. (The right pyeloureterogram in the x-ray was made postoperatively by injection through the ureterostomy tube before removal of the stone from the bladder.)

Too precipitous use of a stone basket is illustrated by the following experience.

A white American widower (A. R. XL67722) farmer by trade, aged forty-seven, entered the Indiana University Medical Center March 9, 1943, complaining of pain of nine days' duration in the left costovertebral angle radiating around the flank into the left lower quadrant, penis and left thigh. The onset lasted three or four days and was characterized by a dull backache. The pain then became sharp and radiated as described. Morphine gave relief. Several relapses occurred before admission. Family history and past personal history were irrelevant save that the patient's father, aged seventy-one, has had renal calculi. Physical examination showed a man of linear type, apparently in much pain. The head, neck and chest were not remarkable. The blood pressure was 120/76. Examination of the abdomen revealed tenderness in the left costovertebral angle and left abdomen. Relevant laboratory data showed a mild secondary anemia, gross hematuria and phthalein excretion 11.5 per cent in forty-five minutes. Blood chemistry was normal. Original roentgenogram showed an opacity 4 by 8 minims in size lying along the course of the left ureter near the vesical juncture.

The patient was first seen by us two days after admission (March 11, 1943). An obstruction was encountered (Fig 6, film 1) 7 cm. above the left ureteral orifice but passed with a Wishard flat elbowed ureteral catheter. Purulent urine was recovered. A Johnson stone basket was passed, grasped the stone and withdrew it to the ureteral orifice, but not quite into view. The cystoscope was removed and the basket secured to the patient's toe with three elastics. Two cubic centimeters of depropanex and thirty minutes of watchful waiting maintained the status quo. The patient was sent to the ward with elastic traction secured to the leg. A second roentgenogram showed the shadow bank down to its original location alongside the upper convergence of the basket's wires.

Heretofore our impatience has never been taxed over twenty-four hours before recovery of the stone. In this instance, therefore, our watchful waiting expanded into the prayerful variety at the beginning of the second day. However, the temperature did not ascend over 100, the white count over 10,000 nor did the excretion of urine decrease disturbingly. During the second twenty-four hours the tension was

applied only part of the time. No morphine was required. The patient voided around the shaft of the basket. The bladder was never palpable nor percussible. There was no costovertebral tenderness.

At the end of the second day we were twenty-four hours out in uncharted waters beyond our personal experience and felt like the Scotch ferryman in a row boat taking two ministers across Loch Ness in a storm who said, "The wee one can pray, but the big one can man an oar."

Accordingly, on March 13, 1943, under ether anesthesia we slipped the sheath of a McCarthy pannendoscope gently over the shaft of the stone basket and then introduced the foroblique lens. With rapidly diminishing equanimity we saw to our distress that the status quo at the end of the first manipulation was maintained except that at the lower or advancing end of the cage one of the wires had broken and was penetrating the bladder to a depth of 5 mm. or so. All attempts to rotate the basket and withdraw it merely embedded the wire further, although we do not believe it ever entered the vesical wall over 1 cm. in depth. We decided that the exigency, which we always warn such patients may occur, was at hand. The stone was in the intramural ureter, too high to be sure of getting it by opening the bladder, and so low that it was in the most difficult locality to approach by the extravesical pelvic route. One manipulative alternative remained before operation and this was to plunge the basket deeper up the ureter (Fig. 6, film 3) in the hope that it would carry the stone higher where the approach would be easier. The broken wire being at the trailing end of this line of march left us with no worries on account of the break from this maneuver. We were moderately successful, carrying the stone up to a point 5 or 6 cm. below the pelvic brim. Ether was maintained and the patient wheeled to the operating room.

After the abdomen had been prepared with tincture of merthiolate and ether, a left, low, Gibson incision was made with the separation of fascia and muscle fibers down to the peritoneum. The peritoneum was then withdrawn medially and without too much difficulty the ureter was palpated by virtue of the steel shaft within it. There was considerably more difficulty in visualizing the ureter, but it was eventually freed up and opened just below the pelvic brim, 1 cm. from the end of the filiform tip of the basket. A No. 6 ureteral catheter was tied onto the outside of the basket and the entire instrument pulled through the patient's urethra and bladder so that the ureteral catheter was delivered into the incision through the ureter at the operative site. By palpation it was determined that the stone was about 7 cm. below the incision in the ureter. Another incision was made at this point and the stone milked out of the incision in the ureter. The lower ureteral opening was closed with one No. 000 suture on an atraumatic needle, and the upper incision in the ureter was closed similarly with two like sutures. The entire incision was closed in layers with one large Penrose drain

down into the retroperitoneal space in region of the ureter. The ureter above the point of the stone was perhaps dilated twice normal size, but not much more than this. Ten cubic centimeters of slightly bloody residual could be aspirated at will through the lower end of the ureteral catheter which was anchored to the penis at the close of the operation and an indwelling catheter was also anchored in the bladder. The patient left the table after a total of four hours of anesthesia in pretty good condition.

The patient had a tremulous but not tempestuous convalescence for one week, the temperature twice ascending to 101. The only complication was a mild ileus which subsided in a day. The temperature remained normal after the end of one week. The urethral catheter was removed nine days after operation (March 25, 1943). The ureteral catheter came out three days later (March 25, 1943) and the Penrose drain removed from the incision the next day. On March 29, 1943, the phthalein output was 57 per cent in forty-five minutes. On the same day chlorazene dressings were applied to the incision because of purulent drainage.

On April 1, 1943 (nineteen days postoperative) cystoscopic examination disclosed No. 20 strictures in the anterior urethra and budbomembranous juncture. Our note says: "Bladder appears normal and this means the left ureteral orifice as well as everything else." Two No. 5 catheters ascended this orifice 32 cm. without difficulty (Fig. 6, film 4). The urine was absolutely clear, no residual being recovered. Urinalysis the next day revealed two to four pus cells per field as the only abnormality in an acid urine. Roentgenogram showed no remaining opacities, the pyelo-ureterogram being normal.

On the twenty-first postoperative day the patient was allowed to sit up, desiring "to leave here as soon as I can find a way to get out." On the twenty-second day he believed he had had his pain because he had not preached religion as he should! The intern's note of the same day stated: "Think patient is on a schizophrenic spree. Wound in excellent condition." The patient was discharged on April 6, 1943, twenty-eight days after admission and twenty-four days after operation. Diagnosis: (1) Left ureterolithiasis (removed) with attendant infected hydronephrosis (relieved); (2) impacted Johnson stone basket (removed).

SUMMARY

Three courses are open in the treatment of stones in the lower third of the ureter: (1) Spontaneous passage under observation is prudent in the face of progress if the stone is not too large, the time required not too long, and the patient not suffering from too severe ureteral obstruction with its attendant stasis and infection. (2) Instrumental passage is safe if coincidental ureteral drainage and dilation is maintained and extraction accomplished with flexible non-

metallic instruments. It should be abandoned in favor of surgical removal if progress ceases or if drainage becomes ineffectual and there is danger of attendant sepsis. The use of metallic extractors introduces hazards which are discussed. (3) Surgical removal should be used for stones which are disproportionately large to pass or extract, or if methods (1) or (2) seem wise to abandon. It is safe and for the most part certain and free from the complications of method (2). In eighteen years we have had no deaths among private patients suffering from ureterolithiasis.

An instance is reported illustrating failure with the extraction method, fracture of the basket and delivery of stone and basket from above.

A LOOPED CATHETER IN THE TREATMENT OF URETERAL CALCULI

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Various ingenious devices have been developed to aid in dislodging and for the purpose of extracting ureteral stones. The use of these has been limited largely to the treatment of stones impacted in the pelvic segment of the ureter. Rapid dilatation by means of bougies or catheters, or by one or more inlying catheters is a safe and, in many instances, an effective method. Various modifications of the catheter technique have been proposed but none is entirely satisfactory and without danger of inflicting more or less serious injury. Dangers inherent to the use of rigid instruments are undoubtedly greater than those with flexible instruments although serious injury may attend the injudicious use of the latter. Twisting ureteral catheters passed beyond the level of the stone in the hope of entangling and extracting it on withdrawal of the catheters as suggested by Bumpus, is a relatively safe method but, in our experience, rarely succeeds, although not infrequently the stone is passed subsequently. The McKay stone dislodger comprises a catheter to which four strands of silk ligature are attached, the purpose being to enmesh the stone on withdrawal of the instrument. Finney suggests tying a silk ligature to the distal tip of the catheter which is then introduced. With the tip of the catheter in the renal pelvis, traction is made on the ligature, thus looping the catheter which on withdrawal may catch the stone and extract it. The Johnson wire stone basket, which seems to be in current favor, is an improvement over the original instrument which was the same in principle but comprised of an ureteral catheter and projecting wires. Among many other devices described is the Zeiss looped catheter which was introduced in Germany in 1937 and described in this country by Wehrbein in 1942. Our instrument is the same in principle as the Zeiss looped catheter, but is, we believe, easier to construct, is equally if not more efficient, and has an added feature of safety.

THE INSTRUMENT

The materials required are an ureteral catheter, a strand of steel surgical suture wire (No. 33 or No. 35) approximately 6 inches longer than twice the length of the catheter to be used, and an ordinary pin. Since it is usually employed in the attempt to extract stones from the pelvic segment of the ureter, the catheter may be shortened to any desired length by removing a segment from its

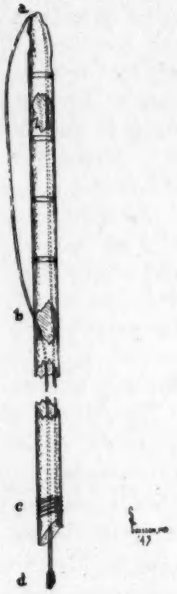

Fig. 1. *a*, Site of perforation where wire enters tip of catheter. *b*, Site of perforation at 5 cm. level where wire again passes into catheter lumen. *c*, Point at which wire which entered at "a" is wound about proximal end of catheter fastening it securely. *d*, Working end of wire which loops catheter when traction is applied.

proximal end. Indeed this is desirable since less wire and effort are required to modify the shorter catheter. The latter should be whistle tipped and either No. 4 or 5F; the former being preferable since it is easier to introduce and less likely to inflict injury. We have been using the plastic ureteral catheter but the woven nylon variety should prove equally, if not more, satisfactory.

Perforations are made, using the common pin, one in the "tip" of the beveled end and another at a point 5 cm. distant from the tip of the catheter (Fig. 1). The ends of the wire are now passed through the perforations into the lumen of the catheter and advanced until they appear at its proximal end. The terminal portion of the wire which entered at its tip is now anchored to the catheter near its proximal end. This attachment must be very firm and this is facilitated by wrapping the wire tightly so as to include the upper portion of an oblique opening at the proximal end of the catheter. The end of the wire which entered the lumen of the catheter at the 5 cm. mark is now pulled upon until its exposed portion near the tip lies snugly against the catheter. Further traction applied to the end of the wire which hangs free, loops the distal end of the catheter. The wire may be knotted to give purchase to the fingers as traction is made on it in forming the loop; however, the knot must be small enough to pass through the perforated rubber tip of the operating cystoscope since it may be desirable to remove the latter, leaving the extractor in situ. When properly made the beveled end fits snugly against the side of the catheter when the loop is completed (Fig. 2).

TECHNIQUE

Simple precystoscopic preparation is desirable. The lower bowel should be emptied. Preliminary sulfonamide therapy is advantageous. A sedative, usually dilaudid, is given. Novocaine solution (5 per cent) is employed for analgesic purposes. With the exposed portion of the wire closely applied to the body of the modified catheter, the latter is passed into the ureter and to a point approximately 10 cm. beyond the level of the stone. Ureteral meatotomy has not been necessary in any of the cases, since the loop insures adequate dilatation. A small amount of mineral oil is injected after which the loop is formed by traction on the free end of the wire. The looped catheter is then slowly withdrawn, at the same time the ureteral orifice is kept under observation. As the stone held in the grasp of the loop enters the intramural segment of the ureter, bulging is noted and at this time the beginning of the loop may be seen projecting through the ureteral orifice. The cystoscope may or may not be removed at this time. There is comparatively little danger of inflicting serious injury at this stage of the procedure so that considerable traction may be applied. It is highly important

to maintain the loop at all times. The calculus may appear firmly caught within the loop which is usually the case when the cystoscope has been removed prior to the final pull, or it may fall into the bladder as the loop is withdrawn. In some instances a second attempt is necessary since the stone may slip out of the loop at a narrow meatus. An indwelling ureteral catheter is used for twenty-four to forty-eight hours postoperatively.

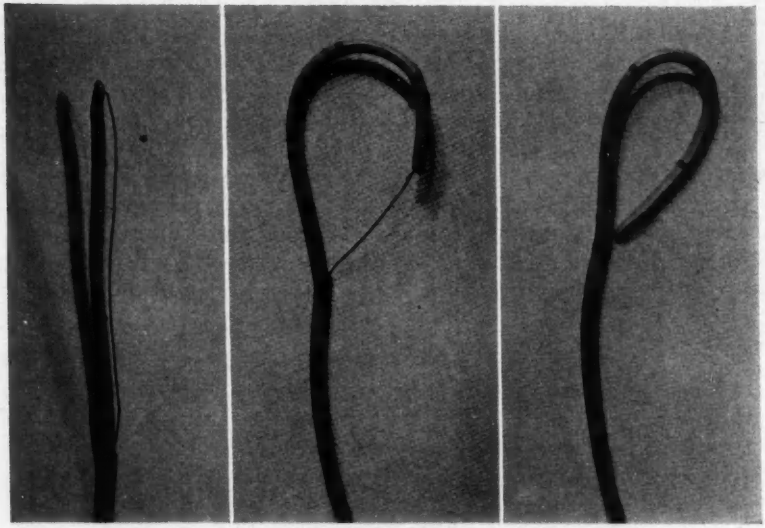

Fig. 2. Distal end of modified ureteral catheter.

COMMENT

The success of this procedure depends primarily on introducing the modified catheter beyond the level of the stone. However, the loop provides an excellent means of dilating the ureter below the level of an impassable obstruction due to stone and when so employed in two cases the stone subsequently came away spontaneously. In several instances, having failed to pass the modified catheter beyond the stone, we succeeded later. These manipulations are remarkably free from pain and forming the loop within the ureteral lumen rarely causes discomfort. This may be attributed in part to ureteral dilatation above the stone. In no case did the patient com-

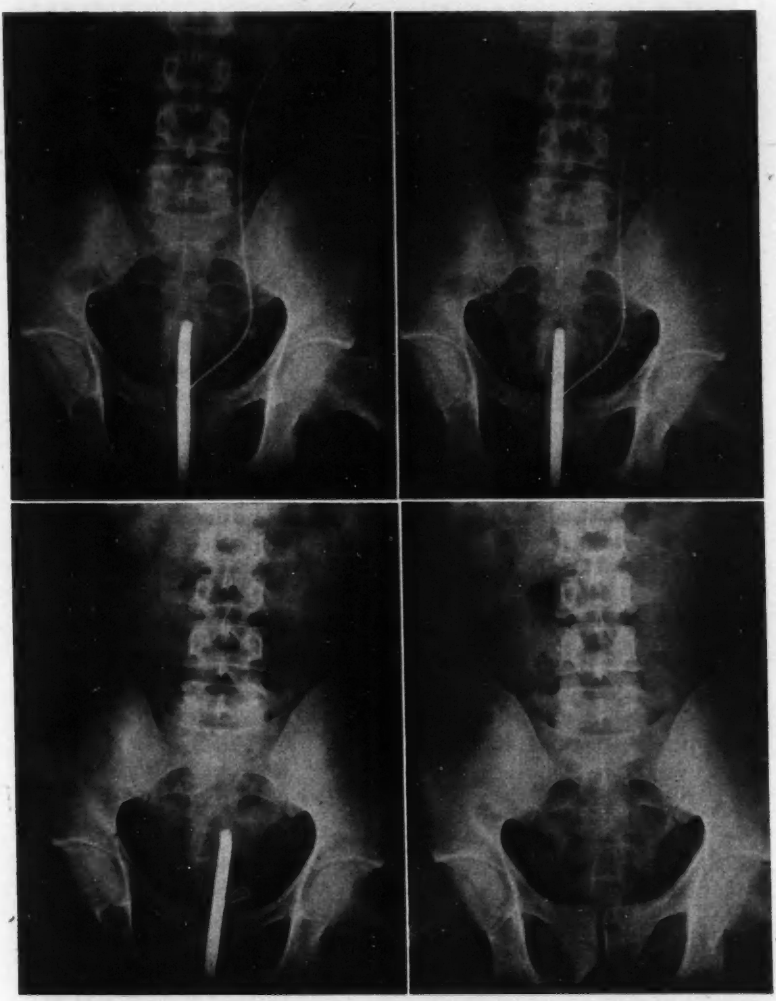

Fig. 3. Upper left: Modified catheter passed beyond calculus, higher than necessary in this case. Upper right: Catheter looped in upper ureter. Lower left: Calculus within loop now in intramural segment of ureter. Lower right: Calculus now removed.

plain of pain or even discomfort while the catheter, with the stone in its grasp, was being withdrawn until the loop entered the intramural segment. Momentary pain is felt when the stone in the grasp of the loop is pulled through the ureteral meatus. Absence of pain in the unanesthetized patient is a positive indication of the absence of trauma; under spinal or general anesthesia this index of safety is removed; we do not employ either. There is the possibility that the maintenance of muscle tone in the ureteral wall in the unanesthetized patient serves to compress the stone within the loop and helps to hold it there.

As mentioned above, meatotomy has not been employed; the dilatation effect of the loop stretches the orifice widely. In several instances the stone escaped the grasp of the loop when traction was made against a tight orifice but came away on the second attempt. Small tears in the orifical mucosa with slight bleeding occurred in every case but no treatment other than the use of an indwelling ureteral catheter was necessary. Continuous traction over a considerable period of time on an arrested loop has not been employed. Should the loop with the stone in its grasp be arrested above the level of the intramural segment, with or without pain, it is our belief that the loop should be opened without delay.

This is accomplished by the simple expedient of detaching the fixed end of the wire and putting traction on the free end. The wire is then removed and the catheter loop freed. The wire having been removed completely, the catheter may be left indwelling or removed as circumstances dictate. This safety feature, together with a conservative attitude on the part of the operator, insures against the infliction of serious injury.

RESULTS

The technique described above has been employed successfully in thirteen consecutive cases. In three of these a second attempt was necessary since the calculus slipped out of the loop at the level of the ureteral orifice. The calculi in all of these cases occupied the pelvic segment of the ureter, the highest one having been arrested 9 cm. above the ureteral meatus. Most of the calculi were small; the largest one measured 1.5 cm. by .6 cm. by 0.4 cm. In two cases the calculi were nonopaque. Without doubt many of these stones would have come away after the conservative use of catheters, but

it is interesting to note that in seven of the thirteen cases ureteral dilatation had been employed unsuccessfully. The history of two of these cases follow.

CASE REPORTS

Case 1.—Mrs. A. A., a forty-six-year-old white woman, was first seen in the outpatient department of the Pennsylvania Hospital in May, 1940. At that time she complained of pain in the right loin and abdomen which had occurred off and on for 3 years. The x-ray disclosed a small calculus in the lower right ureter. Despite many attempts to dislodge the stone, the condition remained unchanged and on two occasions she was admitted to the ward on account of severe attacks of pain and fever. These attacks were easily controlled by catheter drainage, and inasmuch as the calculus was small and the patient very obese, it was decided to continue with conservative measures. Ureteral meatotomy was done on the occasion of her first house admission. B. coli were recovered from the right kidney urine. The patient was readmitted to the ward on March 27, 1943, in a severe attack; despite repeated dilatations with pelvic lavage, some seventeen in number, the position of the stone, which was not encysted, had remained unchanged. On the day of admission a modified No. 5 catheter was passed beyond the site of the stone which was situated 5 cm. from the ureteral orifice, and considerable thick, heavily-purulent urine was recovered. The loop was made with the tip of the catheter at the 15 cm. level and withdrawn bringing the stone with it. All symptoms disappeared after three days and one month later the kidney was found to be normal in function and free from infection.

Case 2.—F. W., a forty-two-year-old white man, had been treated by conservative measures over a period of 5 years for minute bilateral single renal calculi. The stone on the right side entered the ureter in November, 1942, and finally lodged in the pelvic segment at the level of the spine of the ischium where it remained despite many ureteral dilatations. The condition at the time was asymptomatic. Later repeated attacks of left sided pain necessitated pelviolithotomy in January, 1943, the stone having increased considerably in size. Three months after the operation severe attacks on the right side necessitated readmission of the patient. The stone was easily removed by means of the modified catheter. The patient had had seven unsuccessful cystoscopic manipulations in attempts to dislodge the small stone.

Cases, such as the foregoing, in which small calculi remain despite ureteral dilatation present ideal conditions for employment of the modified catheter. We have had no experience with the use of this instrument in the case of very large calculi.

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INTUBATED URETEROTOMY

A NEW OPERATION FOR URETERAL AND URETEROPELVIC STRICTURE

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The surgery of the ureter has lagged behind the surgery of the kidney in a manner that is difficult, now, to explain. Only a few years ago there was a general feeling that the ureter seldom required attention, except for the occasional case where it had to be removed. This perhaps arose from the fact that after pyelography was invented the medium was always injected through a catheter lying in the renal pelvis. This brought about a rapid increase in our knowledge concerning renal pathology, and much of it concerned the effects of obstruction. In conservative kidney surgery, attention centered upon plastic operations on the pelvis, largely ignoring the consideration, which now seems obvious, that the cause of the pelvic dilatation must be an obstruction lying at some point in the ureter. Next, ureteropelvic obstructions were treated by plastic operations, and much argument arose as to the desirability of using a tube splint after such operations.

Hunner's persistent campaign brought the realization that there are many ureteral obstructions below the ureteropelvic junction, and that many of these are amenable to treatment by dilatation. The operative treatment of strictures not responding to dilatation has remained unsatisfactory; in fact, it is seldom attempted.

About ten years ago, when faced with a dense, fibrous, thick-walled stricture of the upper ureter, I applied the principle of the Rammstedt operation for pyloric stenosis, and divided the stricture longitudinally, passing through all the layers of the ureteral wall except the mucosa (Fig. 1).[3] The result was most satisfactory. Good results have since been obtained with this technique by Bidgood and Roberts[1], Gibson[4] and others, and the operation is now generally adopted for the comparatively few cases in which it is applicable.

The question of splinting after ureteropelvic plastic operations came up every time such an operation had to be done. Opinions have varied radically as to the value of the splint. Peck[10], Harris[5],

Cabot[2], Moore[8], Sargent[12] Priestley[11] and Ormond[9] have all favored splinting. Gibson[4] puts the case for splinting as follows: "No matter how generous the surgeon is in the use of sutures in plastic repair, the outcome is likely to be a failure unless he makes use

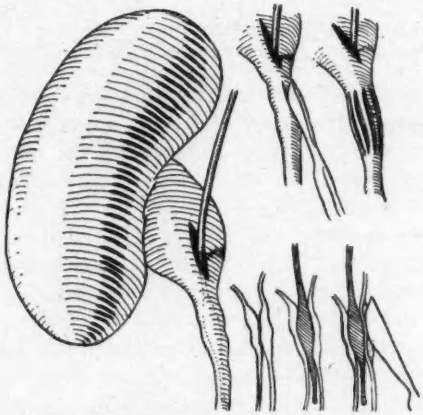

Fig. 1. Rammstedt type operation for thick-walled ureteral stricture. The stricture is stretched by a bougie inserted through a pyelotomy incision; one or more longitudinal incisions are made passing through all layers of the ureteral wall except the mucosa.

of splinting; conversely, if he places his dependence on adequate splinting the result will almost certainly be successful even though he uses no sutures at all." In spite of this, Gibson states that he does not "eschew the use of sutures entirely."

In quoting authorities for the use of the ureteral splint, it should not be forgotten that Albarran recommended that whenever the kidney is opened, as large a ureteral catheter as possible should be passed down the ureter and left in place for several days.

It seemed to me that the results were better in the splinted cases, but splint or no splint, there were all too many failures, partial or complete.

Another aspect of the problem appeared as the result of experiences with urethral strictures. I had occasion, nearly twenty years ago, to operate upon a patient with a very severe bulbo-membraneous stricture, accompanied by extensive perineal scarring and

multiple fistulous tracts. After laboriously dissecting away the scarred, diseased tissue, there was left a huge hole in the perineum, and a narrow ribbon of urethral wall, representing a part of the roof of that organ, bridging a gap in the urethra a good inch and

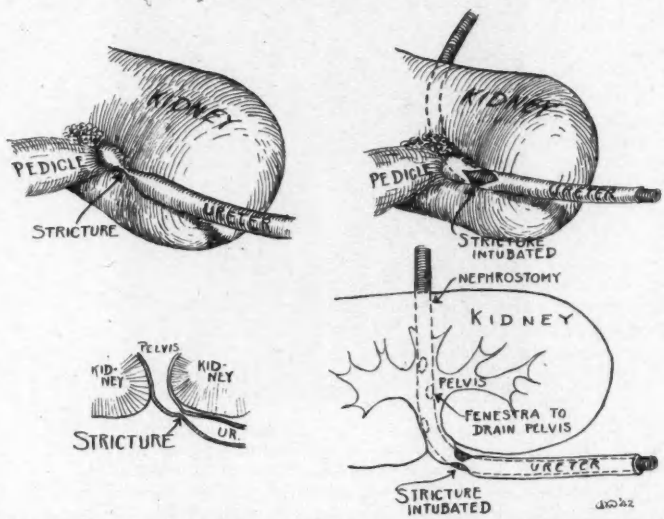

Fig. 2. Case 1. *A*, Conditions at found at operation; *B*, Diagrammatic section through ureter as it entered kidney; *C*, Stricture incised, splint tube in place in ureter, proximal end brought out through nephrotomy incision; *D*, Diagrammatic section showing conditions at end of operation.

a quarter long. I lacked the courage to extend the dissection far enough to permit freeing of the urethra, freshening of its ends, and circular suture in the classic manner. Instead, I passed a No. 24 F. catheter through the entire length of the urethra into the bladder, fastened it in place, and left the wound unsutured. The catheter was visible at the bottom of the cavity for many days, but after two weeks it was covered by healthy granulations. At the end of three weeks it was withdrawn, and the result was so excellent that no later dilatations were required. Evidently, the epithelium had grown around the circumference of the catheter, and a new urethra, healthy and pliable, created. Welland Howard has since described a similar procedure in which he, if necessary,

splits the urethra into several ribbons to permit the passage of the catheter.

In June, 1940, I was confronted by a narrow, thin-walled stricture of the upper ureter just at the point where the ureter disappeared

Fig. 3. Case 1. *A*, Intravenous urogram, pre-operative, showing stricture of upper ureter. *B*, Intravenous urogram, three months after operation, showing stricture no longer present.

into a kidney with a completely intrarenal pelvis (Fig. 2, *A*). The absence of an extrarenal pelvis removed any possibility of using any of the usual plastic operations. The Rammstedt type of operation was out of the question, as the wall of the ureter at the site of the stricture seemed even thinner than the wall of the normal portion of the ureter. At a loss to know what to do, I finally decided to apply the same principle used so successfully in urethral strictures, and to introduce a tube splint which was to remain in place for two or three weeks. A description of this case follows:

Case 1.—Mr. D. B., aged sixteen, in spite of attacks of mastoiditis, sinusitis and rheumatic fever, had usually enjoyed good health. In March, 1940, there was an attack of pain in the right kidney region. This pain recurred fairly frequently, often accompanied by hematuria. There was no frequency.

X-rays taken June 12, 1940, showed a small stone in a lower calyx of the right kidney, and a persistent narrowing of the uppermost part of the right ureter (Fig. 3, *A*). On June 14, a No. 12 F. bulb was

passed to the right kidney, meeting moderate resistance. After this, two or three more attacks of pain, with hematuria, occurred, and x-rays showed the stone to be in the pelvis proper. It was felt that the narrowing seen in the urogram must represent an obstruction, otherwise this small stone would have become engaged in the ureter.

Operation was performed on August 20. The kidney was easily exposed and freed. The ureter was brought up on a tape. The upper portion of it was markedly adherent and was dissected with difficulty until a firm fibrous capsule was split longitudinally. Within this was found a perfect ureter. The pelvis was entirely intrarenal with only a very slight widening at the hilus. The main artery entered the hilus around the side of the ureter. About 15 mm. below the kidney there was a sharp narrowing of the ureter, evidently congenital, as the wall was no thicker than normal and there was no evidence of any inflammatory change in the wall. A small artery joined the ureter at this point. It was doubly ligated and divided. A considerable portion of the fibrous capsule was cut away. Ureterotomy was made all the way up to the kidney, but the hilus would not admit even the little finger. Probes and forceps of all kinds were used to explore the kidney, but the stone could not be located. An x-ray examination was made on the table, and a nephrotomy was made over the stone shadow as nearly as could be made out. In spite of this, the stone could not be found, and further efforts were abandoned in order to avoid damage to the kidney. The ureteral incision was extended down through the stricture. A Rammstedt operation could not be done as the ureteral wall was everywhere of normal thickness. A No. 12 rubber catheter was brought down through the nephrotomy into the ureter. The ureter was closed loosely about it with a suture of No. 000 plain catgut, leaving a considerable defect at the point of the stricture (Fig. 2, *C, D*). It was decided to leave the tube in place at least two weeks in the hope that the ureter would grow around it, thus relieving the stricture, and making it possible for the stone to pass should it again become free in the pelvis.

There was some wound infection with fever. The tube was removed on the fourteenth day, and forty-eight hours later all urinary drainage had ceased. The patient left the hospital on the twenty-seventh day.

On October 17, the patient felt very well, and had no more attacks. The urine contained a few pus cells and some staphylococci.

On October 24, intravenous urogram showed the small stone shadow, apparently in a calyx or in the parenchyma. The upper ureter was well shown, and was uniform in diameter, the persistent narrowing formerly seen being entirely obliterated (Fig. 3).

On August 23, 1942, the patient reported by letter that he was in perfect health, engaging in very heavy physical labor, as well as an active social life, and had never had the slightest recurrence of pain in the kidney.

The excellent result obtained in Case 1 encouraged me to follow the same plan in another similar case.

Case 2.—Mrs. A. K., aged forty-six, had suffered pain in the left kidney since 1917. Calculous pyonephrosis was found in 1925, and

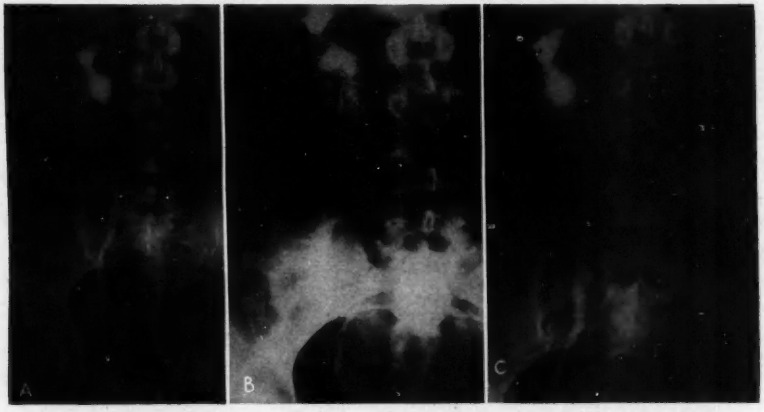

Fig. 4. Case 3. *A,* Retrograde pyelo-ureterogram, pre-operative, showing marked ureteropelvic stricture. *B,* Film made immediately after withdrawing tube. Arrow points to ureteral shadow of wide diameter at site of former stricture. *C,* Retrograde pyelo-ureterogram six months after operation; stricture no longer present.

the left kidney removed. For one year before admission, there was occasional pain in the right back, slight burning on urination, dizziness, and nervousness, but no frequency of urination. There was pyuria, and x-ray showed a stone shadow in the right kidney region. The urine contained many bacilli. Phenosulphonephthalein test was 18 per cent in one-half hour. Pyelography showed an abnormal, irregular, but not particularly dilated pelvis in a large kidney shadow, and a normal ureter. The stone extended to the ureteropelvic junction.

On May 21, 1940, operation was performed. The upper ureter was encased in a thick mass of indurated fat. The pelvis was entirely intrarenal, but the stone fortunately could be removed through a long ureterotomy. The ureter was definitely narrowed below the kidney. A rubber tube, about No. 14 F. in size, and equipped with many fenestra, was passed down the ureter 10 or 12 cm., and brought out through a small nephrotomy incision (same as Case 1). No ureteral sutures were used, and the tube was exposed in the open ureterotomy.

The tube was accidently pulled out on the tenth postoperative day, and there was practically no urinary drainage afterward. The wound

healed per primam. The patient was out of bed on the fourteenth day and left the hospital on the eighteenth day.

A month later 36 per cent of phenolsulphonephthalein was excreted in one-half hour, and the patient felt perfectly well.

Two months later the ureter was dilated with a No. 10 F. bulb. The urine was clear and contained no pus, blood or bacteria.

Later, the ureter was dilated twice, to sizes No. 12 F. and No. 14 F. On July 2, 1942, the patient felt perfectly well, and the urine was clear and uninfected. No postoperative pyelogram has been taken.

Not long afterward a third case presented itself. The situation differed somewhat in that there was a good-sized extrarenal pelvis, and the stricture was considerably longer.

Case 3.—Mrs. B. P., aged twenty-eight, had been troubled with marked pain in her right side since the birth of her first child. Investigations in the hospital showed that the left kidney and ureter were normal, the right kidney pelvis moderately but definitely dilated with a persistent marked narrowing just below the ureteropelvic junction, suggesting an aberrant blood vessel. The ureter below this point was also slightly dilated, suggesting another slight stricture at the lower end (Fig. 4, *A*).

Operation was performed November 19, 1941. The external appearance of the kidney was perfectly normal and it was not adherent, freeing very easily. The ureter, below the kidney, appeared normal. It was brought up on a tape and dissection then carried upward disclosing a marked stenotic area about 1.25 cm. in length just below the ureteropelvic junction. There was no aberrant artery. Above this point the extrarenal pelvis was markedly distended even when the ureter below was quite empty (Fig. 5, *A*). All of the adventitial tissue and blood vessels were dissected away from the stenotic area very carefully. It was found that there were two layers of fibrous tissue completely surrounding the pelvis, and these were divided and stripped away. Pyelotomy was then made, urine spurting out under considerable pressure. The edges of this incision were held up with fine black silk traction sutures. A No. 12 bulb could just be forced through the area of stenosis disclosing the fact that its walls were very thin, even thinner than those of the normal portion of the ureter. A No. 14 bulb could not be passed through the stricture. While the No. 14 bulb was held in place, the ureter was incised longitudinally until the bulb passed freely down into the lower ureter. A small rubber tube about size No. 14 F. was then prepared by cutting the end obliquely, and passed down through the pyelotomy into the ureter to a point about 3.5 cm. below the incision in the ureter. A considerable area of this tube was exposed at the site of the incision. Three fenestra were then cut in this tube so that they would lie in the pelvis. The pyelotomy was drawn together over the tube with one suture of No. 000 plain catgut, but no sutures

were used in the ureterotomy (Fig. 5, *B, C*). The tube was brought out through the upper angle of the incision. The kidney, which was moderately movable, was fastened up to the muscles around the twelfth rib with one capsular suture of No. 2 chromic catgut. The ureter was then seen to lie straight in a normal position.

The patient did very well. The incision healed per primam around

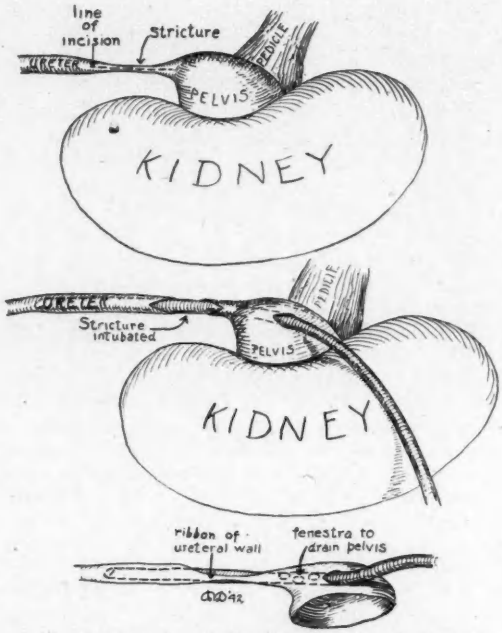

Fig. 5. Case 3. *A*, Conditions as found at operation. The stricture is actually a little below the ureteropelvic junction. *B*, Stricture incised, splint tube in place, proximal end brought out through pyelotomy incision. *C*, Diagrammatic representation of conditions at end of operation.

the tube. The tube remained in place fifteen days, draining considerable quantities of urine. On the thirteenth day it was clamped and remained clamped for twenty-four hours with no leakage about it. There was very slight discomfort at first but this quickly disappeared. On the fifteenth day under the fluoroscope, 12.5 per cent skiodan solution was injected through the tube. It filled the pelvis quickly, outlined the ureter below the pelvis, and entered the bladder. The tube was then withdrawn under observation by the fluoroscope. One could easily

see the upper ureter, and it had at least the same diameter as that below. Following the removal of the tube, no urine leaked through the incision and the patient had no discomfort.

Study of the x-rays showed that immediately after the removal of the tube, the part of the ureter formerly strictured was very well outlined and retained the diameter of the tube at all points (Fig. 4, *B*).

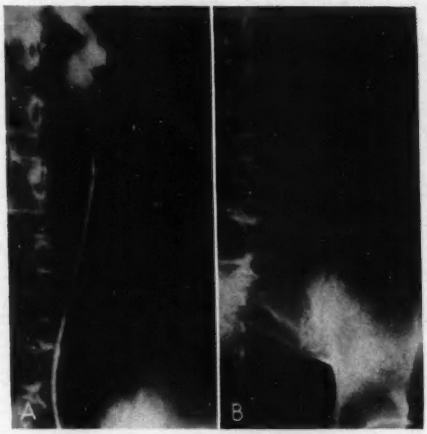

Fig. 6. Case 4. *A*, Retrograde pyelogram, pre-operative, with catheter partly withdrawn, showing normal ureter and ureteropelvic narrowing. *B*, Intravenous urogram, pre-operative. Film taken at one hour and forty-five minutes, showing retention in pelvis.

The patient's pain was entirely relieved. The urine remained clear and uninfected. The lower ureter was dilated on several occasions. On May 18, 1942, the retrograde pyelo-ureterogram shown in Figure 4, *C* was taken, proving that the ureteral stenosis had been completely eliminated. At present the patient is perfectly well.

In the fourth case an upper ureteral stricture was complicated by a membranous valve at the ureteropelvic junction. The operative method was now employed with great confidence as to the outcome.

Case 4.—Mrs. G. I., aged twenty-five, had always been underweight, but enjoyed fairly good health until her first child was born two and one-half years ago. She then developed what was diagnosed as postpartum pyelitis, which persisted. Symptoms of frequency and burn-

ing recurred from time to time, and there was usually a slight afternoon fever. She was examined by Dr. George M. Laws. The infecting organism was B. coli communis. Indigo carmine appeared in eight minutes from the right kidney, and did not appear in fifteen minutes from the right. Retrograde pyelograms showed no evidence of obstruc-

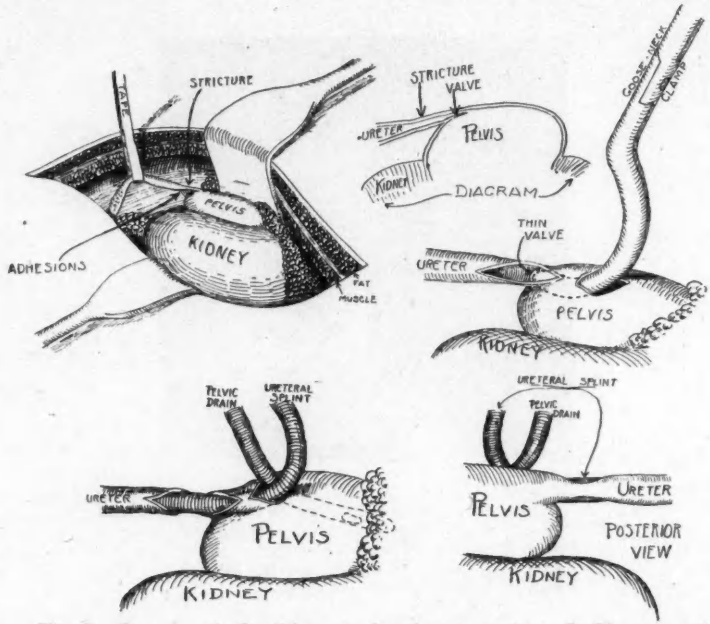

Fig. 7. Case 4. *A*, Conditions as found at operation. *B*, Diagrammatic section of ureter and pelvis, showing stricture and valve. *C*, Valve pushed down into ureter by tip of clamp. *D*, Stricture incised, valve removed, splint tube in place, with proximal end brought out through pyelotomy incision, separate drainage tube in pelvis. *E*, Posterior view at end of operation, showing ribbon of ureteral wall along splint tube.

tion on the right side, but a moderate hydronephrosis on the left, with an essentially normal ureter, suggesting ureteropelvic obstruction (Fig. 6, *A*). Intravenous urography showed a similar picture, with the right pelvis empty after thirty minutes, the left pelvis appearing later than the right and still well filled at one hour and forty-five minutes (Fig. 6, *B*). Treatment with sulfonamides brought about only a temporary clearing of the urine. The slight fever was so persistent that the patient feared she had tuberculosis, and consulted Dr. Burgess Gordon. I saw her on November 24, 1941, at the request of Dr. Gordon, and

Dr. Lewis B. Scheffey. Dr. Laws very courteously made his records and x-rays available. On November 28 cystoscopy showed the bladder, ureteral orifices and urethra normal. Urine from the right kidney showed no pus or bacteria, that from the left side a moderate number of pus cells and numerous clumps of bacilli. Phenosulphonephthalein test: appearance time—right, four minutes, left, four and one-half minutes; collection time—ten minutes; right 14 per cent, left 4.5 per cent; transvesical, trace. It was felt that the condition of the left kidney was sure to grow progressively worse, and operation with the view of relieving the obstruction and saving the kidney was advised.

Operation was performed on December 16, 1941. The lower pole of the kidney was easily freed. The ureter was brought up on a tape and seemed to have a normal appearance. Dissection was then carried carefully up the ureter. There was a small vein in the periureteral fat running to the renal capsule in the lower pole, but this was entirely a capsular vessel and there was no artery accompanying it. It was ligated and divided with no effect on the kidney. It was then possible to expose the pelvis very completely without exposing the upper half of the kidney. Just below the ureteropelvic junction, the ureter narrowed to less than half its diameter elsewhere. There were bands of adhesions joining this part of the ureter to the pelvis, and the lower portion of the pelvis was rounded and projected a little below the ureteropelvic junction (Fig. 7, *A, B*). A small pyelotomy was then made and a gooseneck clamp inserted. In spite of extensive probing it would not enter the ureter but always pushed out the lower portion of the pelvis. The ureter was therefore incised, beginning at the point where the narrowing began. The incision was carried upward until one could see within the ureter the tip of the gooseneck clamp covered by a thin membrane, evidently a congenital valve (Fig. 7, *C*). This was seized with forceps and excised with scissors. The clamp then passed freely down into the ureter. The incision was carried up a little way on the pelvis to insure a widely open ureteropelvic junction. A rubber tube about size 14 F., not fenestrated, was passed through the pyelotomy down the ureter to a distance of about 5 cm. below the ureterotomy. At the site of the ureterotomy, the ureteral wall now covered only about one third of the circumference of the tube. No sutures were used. A No. 16 rubber catheter with the end cut off was then passed through the pyelotomy to drain the pelvis (Fig. 7, *D, E*). The kidney was replaced in position and the tubes arranged so that the ureter followed a normal course.

The convalescence was excellent, and the incision healed per primam. On the fourteenth day there was a transitory episode of fever. On the sixtenth day, acriflavine solution was injected through the ureteral tube and immediately appeared in the bladder urine. The tube was then withdrawn. A short time later mercurochrome solution was injected through the pelvic tube and it was withdrawn. At the next void the urine was highly colored with mercurochrome. There was never any

leakage of urine through the drainage tract. The patient left the hospital on the twenty-second day.

On February 9 and March 2, 1942, catheterized specimens of urine showed no pus or bacteria. The temperature remained normal. An intravenous urogram was made on March 2. The outline of the left

Fig. 8. Case 4. *A*, Intravenous urogram, two and one-half months after operation. Film made at fifteen minutes, showing excellent filling of pelvis. *B*, Film made at one hour, showing pelvis practically empty.

kidney pelvis was much the same as before, but it was well filled at five minutes (Fig. 8, *A*), and completely empty at thirty minutes (Fig. 8, *B*), whereas before the operation it had been still fully outlined at one hour and forty-five minutes. Unfortunately, the ureter was not outlined in any of the films. In July, 1942, the patient stated that she had gained 15 pounds, and felt perfectly well, as she had not for nine or ten years before the operation.

The fifth case was remarkable for the extreme length of the stricture. In spite of previous successes, the operative method was used with some misgivings because of the length of the stricture and especially because the opposite kidney was severely and irreparably damaged. Nevertheless, there appeared to be no other method of

dealing with the situation, which I thought then and still think provided an acid test for the procedure.

Case 5.—Mrs. A. B., aged thirty-two, had suffered severe pain in the right side since April 15, 1941. Attacks recurred about every two weeks, accompanied by chills, fever, frequency and hematuria. Urine was cloudy at all times.

X-ray showed multiple large stones in the right kidney region. Urine showed many white blood cells, few red blood cells, many bacilli.

Cystoscopy was done on March 5, 1942. Urine from left kidney was clear, no bacteria. Phenolsulphonephthalein intravenous showed right, 7 per cent, left, 22 per cent in ten minutes. Left pyelo-ureterogram showed a marked hydronephrosis, the uretero-pelvic junction funnel-shaped, but the upper ureter very small for 10 cm. (Fig. 9, *A*). The catheter met resistance in this region.

The patient became very ill, developing severe pain in the left kidney region, accompanied by chills, sweats and high fever, indicating that infection of the left kidney had occurred. This infection persisted unabated for eight days, in spite of large doses of sulfathiazole, and it became apparent that something radical would have to be done to save the patient's left kidney, her only good one.

Operation was performed on March 13, 1942. The peri-renal fat was adherent and vascular. The ureter was small but thick-walled with a thicker capsule than normal and numerous good-sized veins coursing along it. It resembled a normal vas deferens. About 10 or 12 cm. below the kidney it assumed a normal appearance (Fig. 10, *A*). The extrarenal pelvis was of moderate size and thickened (muscular hypertrophy). Ureterotomy was made in the middle of the narrowed portion. A No. 10 ureteral bulb passed upward to the kidney with great difficulty, and downward with almost equal difficulty until it reached the normal portion of the ureter. It then went easily to the bladder. Efforts to dilate the ureter further were unsuccessful. When sufficient force was applied, the ureter split. It was felt that relief of the obstruction was absolutely necessary to the patient's welfare, as the other kidney would undoubtedly have to be removed. For this reason, the ureter was boldly incised throughout the entire length of the narrowed portion (10 to 12 cm.). This converted this portion of the ureter into a narrow ribbon. The incision was extended upward a little way into the pelvis. One end of the crosspiece of a No. 16 latex gall-bladder T-tube was then inserted in the pelvis. The other end barely reached the lower extremity of the ureteral incision, and was inserted into the normal part of the ureter, and held there by a suture of No. 000 plain catgut (Fig. 10, *B*). The ribbon of ureteral wall was then held in close approximation to the tube by three sutures of No. 000 plain catgut. It did not cover more than one-third the circumference of the tube (Fig. 10, *C, D*). The stem of the T-tube was brought out the upper angle of the wound for urinary drainage.

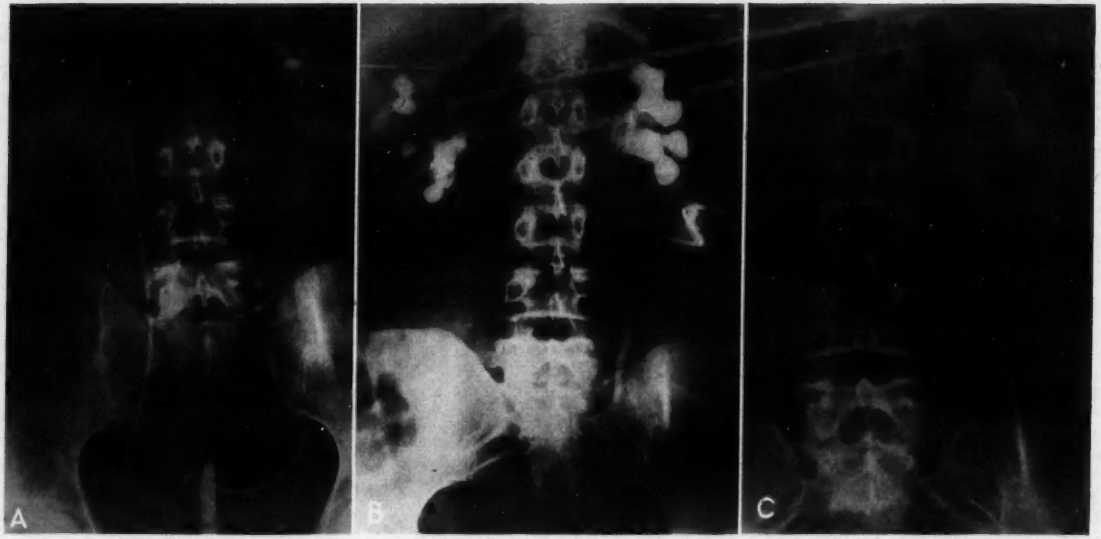

Fig. 9. Case 5. *A,* Retrograde pyelo-ureterogram, pre-operative, showing left hydronephrosis, ureter narrow and thread-like in its upper third, lower two-thirds normal. Note large stones in right kidney. *B,* Pyelogram made by injecting through tube. Note outlines of new-formed ureter alongside tube. *C,* Intravenous urogram made six months after operation. Note widely patent ureter, compare with *A.*

The wound was closed in the usual manner, with two or three rubber tissue drains.

Convalescence was afebrile and uneventful. The wound healed by first intention.

On April 14, skiodan solution was injected through the tube and

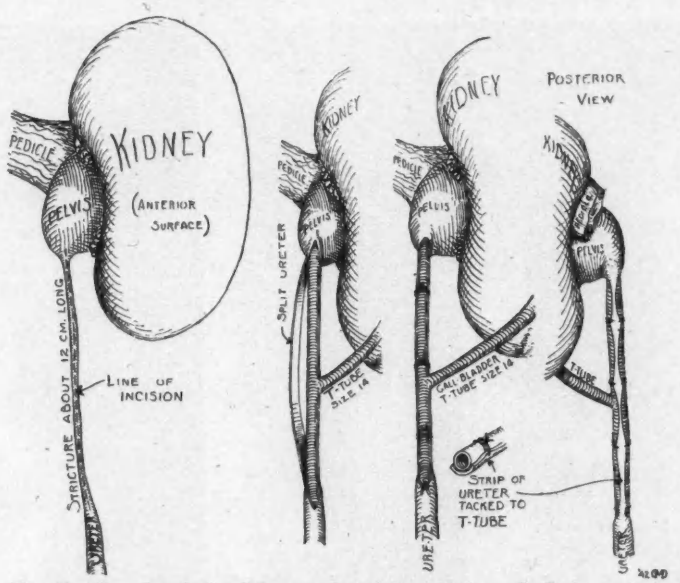

Fig. 10. Case 5. *A*, Conditions as found at operation. *B*, Stricture incised through its entire length, T-tube in place. Note that ureteral ribbon does not stay in contact with tube. *C*, Ureteral ribbon held to T-tube by sutures. *D*, Posterior view, showing ureteral ribbon closely applied to T-tube. Stem of T-tube provides urinary drainage.

the radiograph shown in Figure 9, *B* obtained. The lower limb of the T-tube was evidently occluded, but the solution flowed freely around the tube into the bladder. The tube was therefore withdrawn on April 12, thirty-one days after the operation. No urine drained through the incision, but the temperature rose to 100 F. and the patient had pain in the left kidney. A No. 9 urethral catheter was passed easily to the kidney and left in place five days, when it was withdrawn. There were no further symptoms, and the temperature remained normal.

On April 24, a No. 14 bulb passed to the left kidney with perfect ease, meeting no resistance at any point. The patient left the hospital April 26, 1942.

Later she reëntered the hospital, and on May 19 the right kidney was

removed. It was a useless, thin-walled sac and contained several large stones. The convalescence was uneventful, and the patient left the hospital on June 3.

On July 1, the patient reported for observation. She felt perfectly well. The catheterized urine was clear, and contained no pus, blood

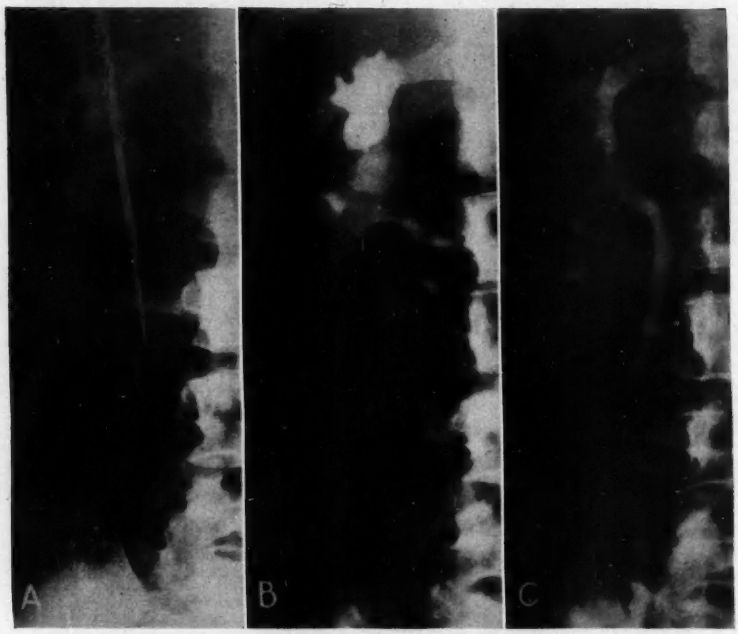

Fig. 11. Case 6. Left panel *(A)* is a retrograde pyelo-ureterogram showing moderate hydronephrosis and definite ureteropelvic stenosis. The middle panel *(B)* is a plain film showing large multiple stones. The right panel *(C)* is a retrograde pyelo-ureterogram taken about six months after operation showing a really remarkable return to normal.

or bacteria. Phenolsulphonephthalein test, intravenous, showed 47 per cent in thirty minutes.

On August 17, a No. 14 bulb again passed to the left kidney with perfect ease.

On September 9, intravenous urography was carried out. The ureter was well outlined, as shown in Figure 9, *C*, and obviously of normal diameter or greater. These findings prove beyond doubt that the new ureter is functioning in a thoroughly satisfactory way.

Case 6.—Mr. M. G., aged twenty-nine years, complained of right renal pain. Examination showed large, multiple, bilateral renal calculi, bilateral hydronephrosis due to ureteropelvic obstruction, and bilateral infection with Proteus. Figure 11, *B* shows the stones in the right kidney; *A* shows the dilated pelvis, normal ureter, and constricted ureteropelvic junction. The stones were removed by nephrotomy; the ureteropelvic stricture was incised longitudinally, and intubated with a No. 16 rubber tube, which remained in place three and one-half weeks. The kidney pelvis was drained with a large nephrostomy tube. Shortly after the operation, a ureteral catheter was passed into the pelvis through the nephrostomy tube, and a continuous Murphy drip irrigation, at first of Albright's solution and later of Suby's solution, kept up for about six weeks. Before the removal of the nephrostomy tube, it was ascertained by x-ray that fluid went quickly and easily to the bladder. The drainage sinus closed quickly. The elimination of the ureteropelvic obstruction and the return of the pelvis to normal is shown in Figure 11, *C*, taken eight months after the operation. On several examinations, the urine from the right kidney had been clear and sterile, a noteworthy result after a Proteus infection. The phenolsulphonephthalein output from the right kidney is normal. The opposite kidney has now been operated upon in a similar manner. The patient's condition is good, but roentgenograms have not yet been obtained to demonstrate the result on the left side.

Case 7.—Dr. C. P., aged sixty years, was ill with tuberculosis at the age of twenty-seven and again at thirty-five. During the last five or six years he has had intermittent attacks of diarrhea and constipation, attacks of pain in the right loin increasing in frequency up to about once a month in the past eighteen months, and sometimes accompanied by nausea. He noticed a lack of energy, and had lost 20 pounds in weight. Intravenous urogram made in another city showed a double but unobstructed kidney pelvis on the left. The right pelvis was moderately dilated, the infundibula widened. The ureter and ureteropelvic junction were not shown at all, as seen in Figure 12. This is the appearance characteristic of ureteropelvic obstruction. The urine was uninfected. On the basis of the history and intravenous urogram, diagnosis of ureteropelvic obstruction was made. Retrograde pyelo-ureterogram added nothing to this. The entire ureter seemed small and spastic. Repeated examinations for tubercle bacilli were negative. Operation was performed October 14, 1942. The lesion found was a stricture of the uppermost part of the ureter extending over about 2.2 cm. This was rather similar to the finding in Case 3. It was treated in the same way but owing to the generally small size of the ureter, it was necessary to use a No. 10 rubber catheter as a splint tube. Urinary drainage was assured by a large drainage tube inserted through a separate pyelotomy wound.

The splint tube was removed at the end of eighteen days. There was never any leakage of urine through the incision. The patient left

the hospital on the twenty-second day. As one result of the operation, he had a mild urinary tract infection which persisted for about a month and then disappeared after a short course of sulfathiazole. Since that time the urine has remained sterile. He regained his strength rather slowly but never had any return of the pain or the symptoms com-

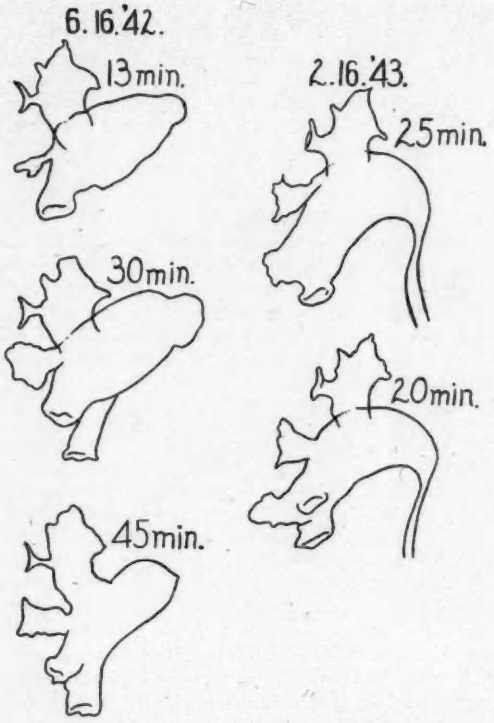

Fig. 12. Case 7. The left column shows three views of the pelvis taken from films of an intravenous urogram series made on June 16, 1942, before operation. The right column shows two pelvic outlines taken from an intravenous urogram series made February 16, 1943, four months after the operation.

plained of in the beginning. An intravenous urogram made February 16, 1943, showed the renal pelvis the same size and shape as before but with a normal-looking ureteropelvic junction and upper ureter in all the films, as illustrated in Figure 12. At this time, he felt very well

indeed; in fact, better than he had for several years. He had regained his normal weight, strength and energy and expressed himself as immeasurably benefited by the operation.

I was unable to find a description of any similar method for treating ureteral strictures until I found, in the 1928 edition of Keyes' Urology a recommendation for "intubation of the ureter" in such situations. Since few details were given, I consulted Dr. Edward L. Keyes personally. He gave me full particulars of a patient he had operated upon in 1915.[6] This case is of sufficient interest to quote in full.

"An able-bodied Irish laborer, whose previous history contained nothing relating to his urinary organs, sat for two hours on a board covered with ice, in February, 1915. Within a few hours he had a severe pain in his left loin, and the next day did not urinate. Alarmed at this, he consulted a physician, who passed a catheter but obtained no urine. Meanwhile the pain had disappeared, and the patient felt perfectly well. So for six days he did nothing, though during that time he passed not a single drop of urine. He then entered St. Vincent's Hospital.

"He said he felt well but he was mentally a little stupid, his superficial capillaries a little congested, his intestines distended, his blood pressure 170, his temperature normal, his left loin slightly tender, but owing to distention the kidney could not be felt.

"The roentgen rays showed a large left kidney but no stone. The cystoscope showed a congestion of the bladder vessels corresponding to the skin congestion. There was not a drop of urine in the bladder. The ureter catheter went up 30 cm. of the left ureter, but drew no urine. A filiform ureteral bougie entered the right ureter for only 5 cm. and drew no urine.

"I therefore immediately cut down upon the right loin but found no kidney there. I turned him over and opened the left loin and found the left kidney very large, congested and tense. I incised the cortex and pushed a tube into the pelvis of the kidney, liberating an ounce or more of urine.

"For two days he was semicomatose and then recovered and made a brilliant operative recovery. For three weeks he passed large amounts of urine daily from the loin tube but none from the bladder. From the bladder washings streptococci were obtained. A second cystoscopy revealed nothing new. Then he began to urinate as much as 700 c.c. in twelve hours. I therefore removed the tube, and in a week the sinus closed, whereupon the temperature went to 105 F. and the loin reopened, so I replaced the tube and left it in.

"In July, five months after the first operation, he returned to the hospital still passing all the urine through the left loin. I reopened

the loin, found the kidney very adherent and the sinus entering the center of the cortex. I mobilized the lower pole subcapsularly, disclosed the adherent pelvis and the ureter moderately dilated below a narrow tight stricture at the ureteropelvic junction. I opened the ureter and found that I could not pass even a probe through the stricture. I

Fig. 13. Case of Dr. Edward L. Keyes. Intravenous urogram made thirteen years after operation. Note widely patent upper ureter.

hoped to do a plastic operation, but found that I could not mobilize the ureter or kidney sufficiently to do so. I therefore made another incision an inch down the ureter and introduced a 20 F. catheter through this up into the pelvis of the kidney, thus splinting the stricture wide open. This tube was left in for three days. Thereafter, most of the urine came from the urethra, but four days later his temperature rose to 104 F. and remained thereabouts for three days, when he passed a small phosphatic stone. His loin then promptly healed and his convalescence thereafter was uneventful.

"Two years later, in July, 1917, after a week of pain and fever in the left loin, he returned. I watched him for ten days, during which he had irregular fever, each relapse of temperature being accompanied by pain in the loin and definite anuria, the longest period of anuria being twenty-four hours. Roentgen rays showed three shadows in the region of the left kidney, two of them regarded as stones. I opened the loin for the third time, found the kidney so bound down

that I could hardly budge it, opened it through the old nephrotomy wound and found but one stone, stuck in the orifice of the perfectly patent ureter. The convalescence was entirely uneventful except that I had to irrigate the pelvis of the kidney once through a ureter catheter to reëstablish ureteral drainage.

"In 1921, five years after his first operation, he remained entirely well, at his work and weighing 200 pounds, but I have had no opportunity to make any examination, except to look at his urine, which showed no pus to the eye."

Dr. Keyes again reported this case before the New York Academy of Medicine in 1940.

On May, 1942, the patient reported himself as still in excellent health twenty-five years after the operation, having had no further treatment in the meantime. Figure 13 shows an intravenous urogram taken in 1928 in which the excellent contour of the upper ureter may be noted.

I also found that McArthur,[7] in 1925, reported the repair of a completely ruptured ureter, with loss of substance. He bridged the gap with a ureteral catheter "of good size." In the accompanying roentgenogram it appears to be a No. 6. The kidney pelvis was drained separately by another tube. The ends of the ureter were drawn as closely together as possible, but failed to meet by one-quarter inch. The splint was left in place nine weeks. The patient became and remained well, but unfortunately no postoperative urine examinations, functional tests or roentgenograms were reported. McArthur used this method because he had tried it successfully in reconstructing the bile ducts. This case is included because the operative procedure is really based on the same underlying principle as in my own operations.

Dr. Keyes assures me that he improvised his operation in 1915, as I did in my first case, for lack of anything better which could be done. The results, in his case, and now in mine, indicate clearly that it is an extremely valuable procedure, that it has wide applications, and that it may be depended upon to produce good effects. The principle involved is quite different from that followed in plastic operations, in which tissues are divided and then reconstructed by sutures in a more suitable form. If the sutures fail to hold the tissues in their new positions until healing occurs, the operation is a failure.

In the intubated ureterotomy, no effort is made to draw the

tissue into a new form, and no sutures are used. The operation depends upon the physiological repair processes of the tissues. The splint is a mold upon which the tissues, by their own proliferation, re-form the ureteral channel in normal size and shape. It must, therefore, be left in place until this proliferation is completed, and the new channel lined by epithelium. The data presented in this paper prove that this actually occurs, and that a new and normal-sized channel replaces the old, strictured one.

One wonders, however, whether the muscular layers of the ureteral wall also proliferate about the tube splint. If not, a considerable segment of the ureteral wall in the operative area would be devoid of muscular coats. Such a new-formed ureter would be incapable of peristalsis, and might interfere with the transport of urine through the ureter. Unfortunately, it has not been possible to perform any experimental work on this problem, and no pathological material is as yet available from any of the patients who have been operated upon. One can only say that urinary drainage from the renal pelvis is free enough so that the urine has become clear and sterile in six of the reported cases, and possibly in the other, and that intravenous urograms give no evidence of any urinary stasis due to changes in the ureter (Figs. 3, 8, 9*C*, 12, 13).

In the use of a ureteral or ureteropelvic splint, the size of the splint, its shape, and the length of time it is left in place are the most important points. I believe that many tubes used as splints have been too small. It seems reasonable that a tube used for this purpose should be as large as will enter the uncut, or presumably normal, part of the ureter without fitting so tightly as to cause ischemia of its wall. It may well be that specially-shaped splints, including perhaps conical ones for the ureteropelvic junction, will prove to be useful. If a splint is withdrawn too soon, it will fail of its purpose. The allowance of time for the tissues to reconstruct themselves about it should be generous, erring on the side of too long rather than on the side of too short. Three weeks may be enough, but should be regarded as a minimum. I believe it will seldom be necessary to leave a splint in place more than four or five weeks.

This method is presented in the expectation that it will prove to be a very valuable means of dealing with all kinds of ureteral and ureteropelvic stenoses, including those not amenable to any other

method of treatment. Indeed, in the Jefferson Hospital Urological Department, operations done according to this method have entirely superseded all plastic operations on the ureter and ureteropelvic junction. We find the technique much simpler, the results much more certain. The provisions of fully adequate, continuous drainage for the urine during the period the splint tube remains in place are essential to success. If this is done, there are remarkably few complications and difficulties.

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RE-IMPLANTATION OF THE URETER INTO THE BLADDER

REPORT OF A METHOD APPLIED TO TEN PATIENTS

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Not many years ago, most urologists viewed with skepticism the advisability of re-implantation of a severed ureter into the bladder. However, we believe the value and the vital necessity of this operation in preserving renal tissue is now generally recognized, and our questions revolve chiefly about the method or methods best suited to achieve this aim.

The need for the operation is apparently most frequent in bladder resections for neoplasm involving a ureteral orifice; but it will be employed in the occasional cases of accidental injury to a ureter (following surgery, labor or other traumatism), of obstruction of the lower ureter due to intrinsic or neighboring disease or to diverticulum of the ureter or bladder, and less frequently in certain instances of ureterocele or extravesical opening of the ureter.

Obviously, there must be enough ureter remaining to permit anastomosis without tension, and there must be in the kidney enough parenchyma to make the operation worth while. Badly infected bladders or ureters may be further contra-indications. There is general agreement in the literature that secondary obstruction causes most of the late bad results, produced chiefly by infection *per se* or as the forerunner of fibrous tissue formation, with recurrent neoplasm playing an important rôle in some cases. We find that dilation of the ureter and particularly thickening (inflammatory or muscular) of its wall, may lead to unsatisfactory anatomic results, although renal function may be largely preserved by the operation.

A considerable, though not exhaustive, review of published reports has been made. The methods employed may be divided roughly into two groups—with the ureter (a) running directly into the bladder lumen through a stab wound, or (b) entering obliquely

according to nature's usual rule governing the entrance of conducting tubes into cavities. Lack of tension is universally recognized as essential. Sutures are sometimes placed outside the bladder, through the ureteral and bladder walls; sometimes they are used only within the bladder; or they may be placed both inside and outside the bladder. Within the bladder, the end of the ureter

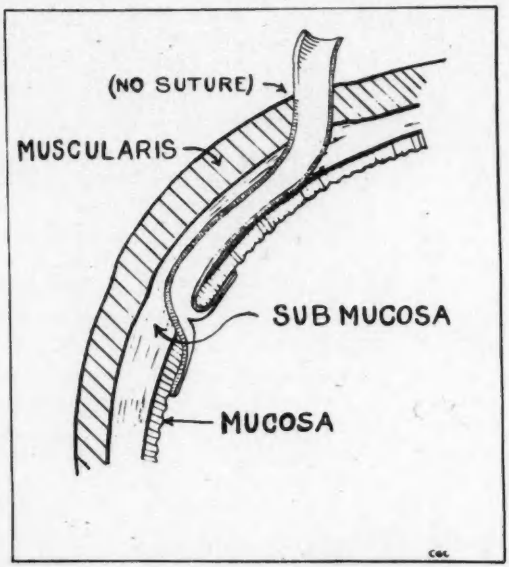


Fig. 1. Diagram of method of re-implantation of the ureter in the bladder.

may be slit on one side only, to make a long elliptical opening, and the end fastened to the bladder mucosa and submucosa only or by penetrating sutures to the whole thickness of the bladder wall. Or the distal centimeter of the ureter may be split in two, and each flap be secured to the bladder; and many advise in addition, further suturing of the ureteral wall to that of the bladder, on each side, at the point of emergence of the ureter in the bladder lumen. Another method, apparently first advised by Furness,[2] permits the end of the ureter to project freely in the bladder, depending on outside sutures only for fixation; ultimately there is found a small protu-

berance or bud. All these methods and variations of them have their advocates.

Patton[5] drew the ureter through the original intramural ureteral channel and fastened the ureter both inside and outside the bladder. Toulson[6] brought the ureter directly through the bladder wall, split the ureter and secured each flap by sutures placed through the

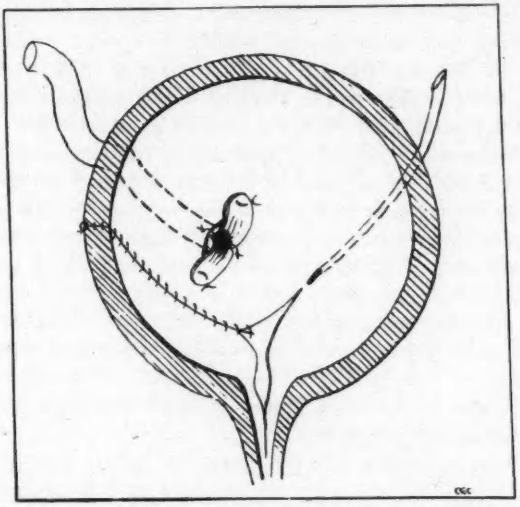


Fig. 2. Diagram of intravesical view of ureteral re-implantation following bladder resection.

bladder with knots on the outside; he scarified the bladder wall under the ureteral flaps to encourage fixation; one suture was placed through the ureteral wall, fastening it to the outside of the bladder; finally, the bladder was "drawn about the ureter, affording something of an oblique entrance into the bladder." More recently Hess[3] has described an intracystic type of re-implantation, applicable to but few selected cases of low ureteral stricture. Practically all authors stress the importance of an extraperitoneal approach (for fear of leakage), the minimizing of infection, the avoidance of tension, and the advisability of placing the bladder at rest by suprapubic or urethral drainage.

Considerable experimental work has been done on dogs, a review

of which is not necessary now. The conditions are quite different from those in man. The bladder in dogs is an intraperitoneal organ, hence the operation must be intraperitoneal; the musculature is relatively much thicker; and the bladder must be closed and the wound sutured tight, hence the bladder is not put at rest. Some observations of Vermooten[7] and associates are pertinent to this discussion. They tried oblique transplantation of the ureter by Coffey's uretero-intestinal technique, incising the bladder musculature, placing the ureter in the submucous trough and carrying it through the bladder mucosa at the distal end of the trough, then suturing the muscle over the trough. Three animals thus operated upon died of peritonitis. Then a series of experiments utilized the same principle of oblique implantation by carrying the ureter through a direct opening and laying it in a trough on the inside of the bladder by incising the bladder mucosa, and finally sewing the mucosa over the ureter, the end of which entered the bladder lumen at the distal end of the trough. This was much more satisfactory. Then a series of ten dogs had one ureter re-implanted by this technique and the other by direct implantation. The comparison of late results was definitely in favor of the oblique entrance. Another observation of these authors indicated the possibility of ureteral dilation in certain instances "due to infection without any demonstrable obstruction to the ureter."

In our laboratories a small number of dogs (eight) have had the ureters re-implanted in the bladder by several techniques. Unfortunately, the pressure of other work interfered with planned experiments. The number of animals in each operated group is too small to permit of conclusive deductions, and the references will be brief.

One dog had bilateral simultaneous re-implantation of the ureters to the bladder through an oblique canal, imitating the Coffey I method of uretero-intestinal anastomosis, using vitallium tubes in the submucous channel. Two weeks later, the blood urea nitrogen was normal (11.5). The animal was sacrificed two and a half months after operation. The vitallium tubes were lying free in the bladder, with no incrustation, and both ureters were slightly dilated and slightly thickened. This type of experiment possessed no clear advantage, and was not repeated.

Three dogs had one ureter only implanted in the bladder by the

same method, omitting the vitallium tube, and a fourth animal had both ureters similarly implanted with an interval of two weeks between operations. All dogs were sacrificed for necropsy, two after a few months and two after eleven months. All transplants were satisfactory and all five ureters and renal pelves showed no dilation. These few experiences were certainly favorable for the Coffey I method used in the bladder.

We questioned whether it was necessary to incise the bladder muscle to make a channel, and three animals were operated upon by the method which will be described later, as used by us on human patients, making the submucous channel by blunt dissection. The first died of peritonitis. The second was in poor nutritional state and died three weeks after operation, badly emaciated. Autopsy disclosed no specific cause of death; the anastomosis was satisfactory and the ureter was not dilated. The third experiment of this group is perhaps worth more comment. We were particularly desirous of learning just what happened to ureteral flaps fastened over bladder mucosa. This third dog had both ureters re-implanted, with four weeks intervening between operations. A month later the blood urea-nitrogen was normal and excretory pyelograms showed normal pelves and ureters. The animal was sacrificed five weeks after the last operation, and both ureters and pelves were found normal in size. It was interesting to note that the ureteral strips fastened over the bladder mucosa at the first operation were now tiny nodules covered with mucosa directly connected with the bladder membrane, and a similar condition with larger nodules was found on the other side. Microscopically one noted the continuity of epithelium between ureter and bladder, with no clear line of demarcation, and indeed no abnormal fibrous tissue was seen about the junction.

The late Edwin Beer[1] forcefully drew the attention of the profession to the value and importance of re-implantation of the ureter to the bladder in certain cases by a publication in 1933, reporting a series of forty-one patients so treated, nearly 75 per cent having had bladder resection for carcinoma. He quoted various authors, particularly among the French, who had expressed very pessimistic views. From the same clinic, Hyman and Leiter[4] had by 1940 increased the series to sixty cases. No attempt was made by them to produce an oblique or valvular implantation; the end

of the ureter inside the bladder was sutured to the bladder, and the ureteral wall was further anchored to the bladder wall as it entered, by two sutures. Of twenty-seven cases controlled by excretory pyelograms, 44.4 per cent had good results, 26.0 per cent fair functional results and 29.5 per cent were classed as poor functional results. Of eleven cases having postoperative cystograms, eight had no reflux up the ureter operated upon, two had reflux up the opposite side and one had reflux up both sides.

Just skepticism was expressed of many reports which were made before the days of excretory urography. Many of the kidneys involved may have become functionless. Yet some of the earlier apparently successful cases were substantiated by chromoscopy and even ureteral catheterization, which demonstrated good renal formation. But there was no way to estimate the anatomic result. Now excretory urography affords at once an answer to both queries.

Realizing that obstruction is a large factor in vitiating results, and that infection also plays a major rôle, we have been trying a simple technique during the past three and a half years, applying many of the above mentioned principles. The operation is always extraperitoneal. Drains are so placed that only rubber tissue contacts the tissues to diminish fibrous tissue formation, and the drains are removed early. Tension is avoided. Sutures are used inside the bladder, penetrating mucosa and submucosa only, and the bladder has been kept at rest by suprapubic drainage. Fine chronic sutures (No. 0000) are used, and we have noted no deleterious results from having the knots within the bladder. Sulfadiazine is used to control infection. In two cases we used one suture outside the bladder, placed in the periureteral tissue, but otherwise none was employed in this situation as it seems probable that suturing of the ureteral wall would encourage the formation of fibrous tissue and might also interfere with intrinsic blood supply.

The operation (Figs. 1 and 2) is done as follows: A small incision is made at the appropriate place on the bladder wall, penetrating muscle only; a rather pointed curved clamp bluntly dissects a channel under the mucosa downward towards the bladder outlet for about 2 centimeters; a small incision is made through the mucosa over the end of the clamp; working through a suprapubic bladder opening, another clamp is passed retrograde through this chan-

nel, and grasps the ureter, the distal centimeter of which has been bisected, forming a "fish-mouth." The ureter is drawn into the bladder through this submucous channel, and the two ends are each fastened to the bladder mucosa and submucosal tissues by a suture of No. 0000 chromic catgut; finally, at each of the two angles between the ureteral flaps, a similar suture is placed through the mucosa and submucosa of the ureter and bladder, trying to avoid muscular layers. No other sutures are placed. This affords enough fixation, if the ureter is under no tension. No catheter is placed in the ureter. A cigarette drain with no gauze exposed is placed near the junction of the ureter and the bladder, but the withdrawal of this is begun the day after operation.

Brief protocols of the ten patients upon whom this operation was performed are given. One patient, apparently doing well, died suddenly the night of operation; no autopsy was obtained. There were no urinary fistulæ and no abscess was found in any patient. All ureters functioned well. Nine patients had resection of the bladder for carcinoma, and one for long-standing fibrous obstruction at the lower end of the ureter. Photographs of the excretory pyelograms of the nine surviving patients are shown—before operation, about three or four weeks after operation and (in all but one) three months or more after operation. The earlier postoperative roentgenograms all indicated some ureteral dilation, but the late ones (eight cases) were of more interest and value. Of three patients with some preoperative ureteral and/or pelvic dilation, two presented the same condition after operation, and one showed increased dilation possibly due to recurrent neoplasm. Of the six patients with no preoperative dilation, one had no late pyelogram, three showed no dilation in the later postoperative roentgenograms, one showed very slight dilation and the fifth had evident hydro-ureter and hydropelvis as late as eight months after operation but none sixteen months after operation. This man (Case 6) entered the hospital later with a bladder papilloma adjoining the prostatic border anteriorly, but with no evidence of growth about the new ureteral opening, on rectal palpation nor by cystoscopy.

Function of the kidney associated with the re-implanted ureter, as indicated by the excretion of diodrast in five-minute roentgenograms, was as good or better than it was before operation in all

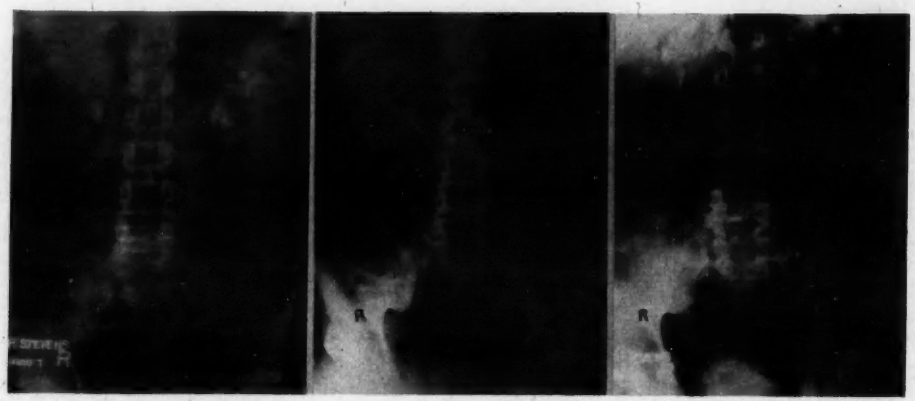
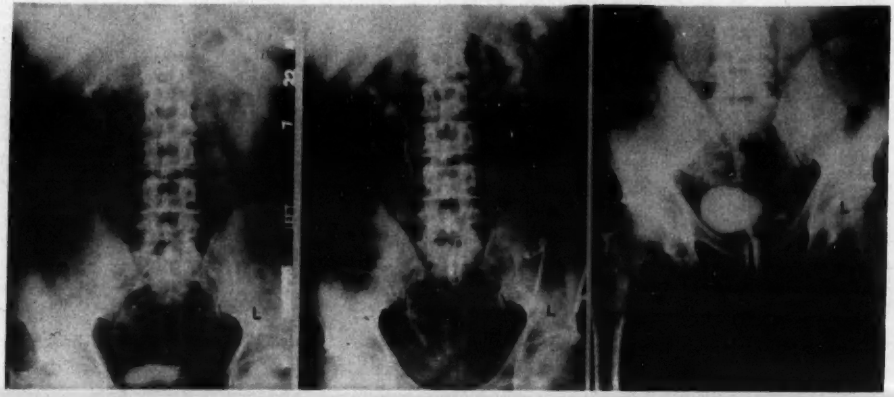


Fig. 3. Case 1. G. H., forty-nine years old, right ureter. (a) Pre-operative view; (b) six weeks following operation; (c) one year following operation.



cases. There were no postoperative symptoms or abnormal signs in the kidney except for one attack of possible mild pyelonephritis in Case 2.

We have postoperative cystograms on only four patients. Case 10 with long-standing ureteral dilation and thickening due to fibrous obstruction and with no postoperative improvement in this regard (although the pain symptom was relieved), showed slight reflux eight months after operation. Case 2 showed reflux a few weeks after operation (rather early observation). Case 7 showed no reflux fifteen months after operation, and Case 6 had none sixteen months after operation.

CASE REPORTS

Case 1.—G. H., a forty-nine-year-old man, was admitted in January, 1940, with transitional cell carcinoma of the bladder. Resection of the bladder was carried out with re-implantation of the right ureter by the technique advocated above. Postoperatively the wound was infected and a secondary closure of the cystostomy was carried out. The right upper urinary tract functioned well and has caused no symptoms in the ensuing three years. There was no evidence of recurrence of neoplasm, and cystoscopy showed normal bladder wall after three and a half years. Normal excretory urogram was found after one year.

Case 2.—G. D., a sixty-four-year-old man, was admitted in July, 1941, with recurrent bladder carcinoma after treatment with radium elsewhere through a cystotomy wound. The patient was diabetic. A bladder resection with re-implantation of the left ureter was carried out by the technique described. The pathologist's report was "papillary transitional cell carcinoma of the bladder." The postoperative course was satisfactory. The cystostomy tube was removed on the thirteenth day. The patient was discharged with a dry wound on the thirty-fourth postoperative day. Follow-up examinations were not carried out by us as the patient returned to his home in Haiti. He died eight months later, apparently of carcinoma. Postoperative cystogram showed reflux up the transplanted ureter four weeks after operation. The excretory urogram showed some pelvic dilation twenty-seven days following operation.

Case 3.—G. M., a fifty-three-year-old man, was admitted in October, 1941, with a carcinoma of the bladder about the size of a dime adjoining the left ureteral orifice. Mild left hydronephrosis and hydroureter were present. Bladder resection with re-implantation of the left ureter was performed by the procedure described. The pathologic diagnosis was "transitional cell carcinoma" and the tumor was found to have invaded the lower portion of the ureter. The postoperative course was uneventful except that the cystostomy closed slowly because of

Fig. 5. Case 3. G. M., forty-one years old, left ureter. (a) Pre-operative view; (b) twenty-seven days following operation; (c) seventy-seven days following operation.

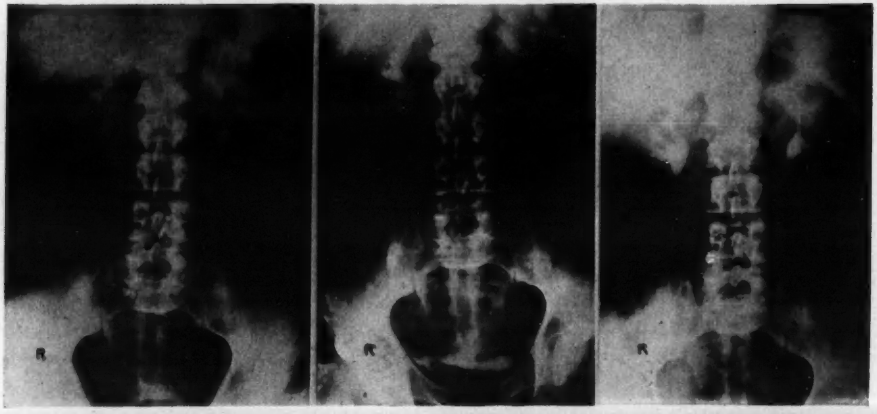


Fig. 6. Case 4. P. L., sixty-two years old, right ureter. (a) Pre-operative view; (b) twenty

mild obstruction from an enlarged prostate. The patient was re-admitted three months later and a single cyst of the right kidney was partially excised. Urinalysis at this time was normal. There were no symptoms referable to the left upper tract. Pyelograms up to that time showed a moderately hydronephrotic left upper urinary tract. Regular cystoscopic follow-up examinations were made, and one year from the time of the original operation a recurrence was found. Subsequently, the patient developed carcinomatosis. Uretero-intestinal transplantation and thoracic chordotomy were done with some palliation. We feel certain that the eventual disappearance of function of the left side was due to the massive tumor recurrence.

Case 4.—P. L., a sixty-two-year-old man, was admitted in October, 1941, with a transitional-cell carcinoma of the bladder near the right ureteral orifice. A bladder resection with re-implantation of the right ureter was carried out by the method described. His postoperative course was satisfactory, though the cystostomy healed slowly. A course of sulfadiazine was given. The patient was discharged in good condition on the forty-ninth postoperative day. He has had occasional pain in the right flank, never lasting over a few hours. The last urine examination found twenty-five white blood cells per high power field in a centrifuged specimen. Tiny papillomata were fulgurated cystoscopically one year postoperatively. Excretory urograms demonstrated slight dilation of the right pelvis, four and a half months following operation.

Case 5.—F. C., a forty-seven-year-old man, was admitted in October, 1941, with a bladder tumor. Complete study found the patient in good condition except for the lesion near the left ureteral orifice. Under general anesthesia, bladder resection and re-implantation of the left ureter were carried out by the method outlined. The specimen removed measured 6 x 4 x 2.5 cm. The pathological diagnosis was "transitional cell carcinoma of the bladder." Approximately four hours after operation the patient was conscious and apparently in good condition when he suddenly became cyanotic and expired within five minutes. Autopsy was not performed. Death probably was due to massive pulmonary embolism. There seems to be no reason to believe that the specific technique of the re-implantation had any connection with the fatal outcome; the ureter was not dilated before operation.

Case 6.—J. M., a forty-one-year-old man, was admitted in February, 1942, with a transitional cell carcinoma of the bladder near the left ureteral orifice. Bladder resection and re-implantation of the left ureter was carried out. Except for a non-specific postoperative epididymitis, the postoperative course was entirely satisfactory. The patient was discharged in good condition with wound healed on the twenty-seventh postoperative day. Subsequently recurrent papillomata have been fulgurated cystoscopically. Seven months following operation, intravenous indigo carmine appeared in three minutes from the right ureteral orifice

Fig. 6. Case 4. P. L., sixty-two years old, right ureter. (a) Preoperative pyelogram (b) pyelogram

Fig. 7. Case 6. J. M., fifty-three years old, left ureter. (a) Pre-operative view; (b) twelve days following operation; (c) eight months following operation; (d) sixteen months following operation.

and in five minutes from the left neostomy. Excretory urograms show moderate pelvic dilation eight months after operation—cause undetermined. Sixteen months after operation the excretory pyelogram is within normal limits. At a subsequent cystotomy the neostomy was easily catheterized and could clearly be seen to pass obliquely through the bladder wall. A cystogram found no ureteral reflux.

Case 7.—F. M., a fifty-four-year-old man, was admitted in January, 1942, complaining of terminal hematuria of four and one-half months' duration. Cystoscopy revealed a slightly raised, flat surfaced, ulcerated lesion approximately 3 cm. from the right ureteral orifice. Biopsy report was "epidermoid carcinoma of the bladder." Complete investigation found no other abnormalities. A bladder resection was done, removing tissue 6 x 4 x 1 cm. in the center of which the lesion was found to be 1.5 x 1 cm. The muscle, however, was not invaded. The pathological report on the operative specimen was "transitional cell carcinoma of the bladder." The right ureter was re-implanted into the bladder by the technique described above. Except for temperature elevation (due to a mild bronchopneumonia) the first three days, the postoperative course was uneventful. The cystotomy tube was removed on the fourteenth postoperative day. The patient was discharged with a dry wound on the thirtieth postoperative day. A course of sulfadiazine was given. Subsequent visits to the clinic have demonstrated a completely satisfactory course. The last cystoscopy done one year after operation found no evidence of tumor, complete healing, and clear urine. Nine months following operation indigo carmine injected intravenously appeared simultaneously from both sides in good concentration in two minutes. Cystogram demonstrated no ureteral reflux. Excretory pyelograms show no dilation of the operated side.

Case 8.—R. V., a thirty-year-old man, was admitted in February, 1942, with a large papillary tumor of the bladder between the left ureteral orifice and the bladder outlet. Total cystectomy was refused at this time. A bladder resection with re-implantation of the left ureter into the bladder was carried out by the technique described. Subsequently, radon seeds were implanted in the suture line. Eventually, recurrences were found. Later bilateral uretero-intestinal transplantation and total cystectomy were done and the patient has returned to work. The re-implantation of the left ureter following resection of the bladder was satisfactory and the patient never had symptoms referable to this. Intravenous pyelograms demonstrate the good anatomical result.

Case 9.—F. A., a fifty-three-year-old man, was admitted in August, 1942, with an epidermoid carcinoma of the bladder just over the left ureteral orifice. A bladder resection and re-implantation of the ureter were done by the technique described. Except for a mild wound infection the postoperative course was satisfactory. The patient was discharged with wound healed on the twenty-eighth postoperative day. He

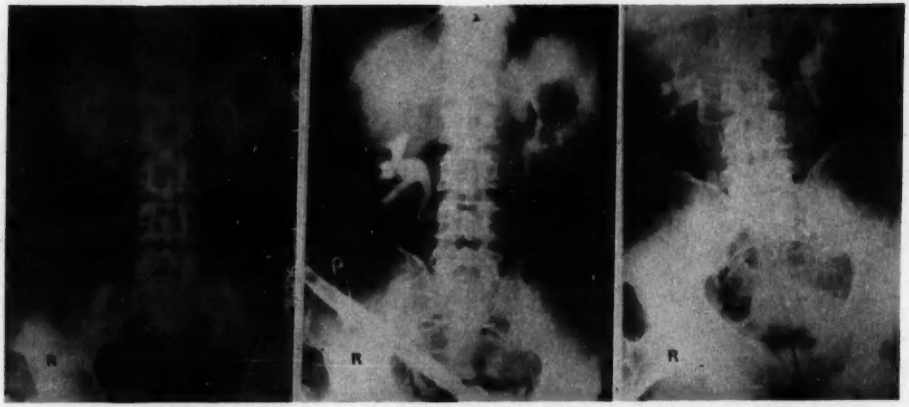


Fig. 8. Case 7. F. M., fifty-four years old, right ureter. (a) Pre-operative view; (b) twelve days following operation; (c) three months following operation.

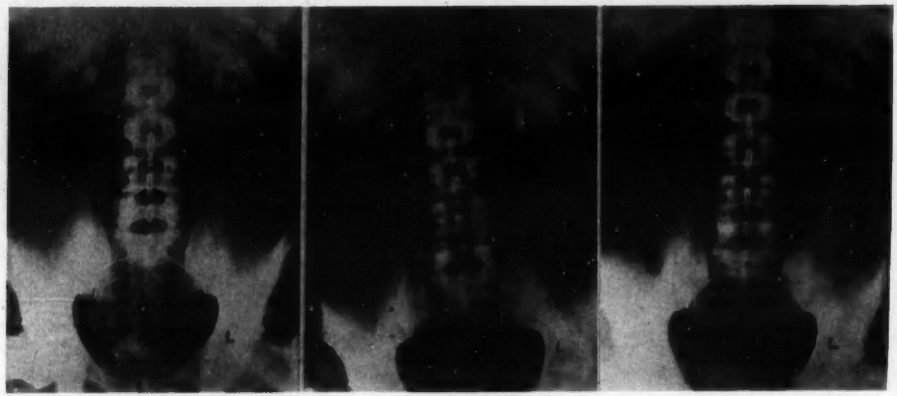


Fig. 9. Case 8. R. V., thirty years old, left ureter. (a) Pre-operative view; (b) forty-

was re-admitted four months later with symptoms of left pyelonephritis which promptly subsided. As can be noted in the pyelograms, the hydronephrosis had increased. A local recurrence of the tumor seemed quite likely, as induration could be made out rectally in the region of the re-implantation. Cystoscopically, however, no recurrence could be made out five months following operation, and intravenous indigo carmine appeared in good concentration from the right ureteral orifice in eight minutes and from the left neostomy in nine minutes. At the time the patient was symptom free. Excretory urograms demonstrate marked hydronephrosis.

Case 10.—R. R., a thirty-nine-year-old woman, was admitted in August, 1942, with pain in the right flank, for surgical treatment of right hydronephrosis and hydro-ureter. Ureteral meatotomy and dilations had been given a thorough trial without effect. At operation considerable heavy fibrous tissue was found about the uretero-vesical juncture which seemed to cause the obstruction by constricting the ureter. The ureter generally was thickened and fibrous. Re-implantation of the dilated ureter was done. The postoperative course was satisfactory and the patient was discharged without pain, in good condition, with wound healed on the thirty-first postoperative day. Seven months after operation there were normal urinalyses and marked symptomatic relief, although occasional mild right flank pain was reported. The patient had gained twenty-two pounds. The pyelograms show but little improvement. The normal urinalysis after three months without drugs, however, seems the clear objective evidence of improvement, as we had had evidence of persistent pyuria for four months before operation.

Fig. 9. Case 8. R. V., thirty years old. left ureter. (a) Pre-operative view; (b) forty-

RESUME

The value of re-implantation of the ureter in the bladder is generally recognized. The type of cases in which it is employed and the various methods advised are discussed.

Some experimental work is referred to, including a few applications of the operations employed by us in man the past few years.

The details of that operation are given, with brief protocols of ten patients. Nine of these had carcinoma of the bladder and one had low fibrous ureteral obstruction. Pre-operative and postoperative urograms demonstrate little or no dilation of the upper tract following operation in five patients having normal urograms before operation. Ureters dilated before operation have remained so afterward. Increased ureteral dilation as noted in the late postoperative pyelogram was seen but once (Case 9) and this patient had probably local recurrence of carcinoma. There were no perivesical abscesses or fistulæ.

Fig. 10. Case 9. F. A., fifty-two years old, left ureter. (a) Pre-operative view; (b) thirteen days following operation; (c) four months following operation.

Fig. 11. Case 10. R. B., female, thirty-nine years old, right ureter. (a) Pre-operative view;

In all patients, function of the kidney on the operated side, as demonstrated in the five-minute roentgenogram of the excretory urogram series, was as good after operation as before, or better.

Postoperative cystograms in four cases show no ureteral reflux in two instances, some months after operation; slight reflux in one patient, who had had a dilated and thickened ureter above a fibrous obstruction, eight months after operation; and definite reflux a few weeks after operation in the fourth case.

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Fig. 11. Case 10. R. R., female, thirty-nine years old, right ureter. (a) Pre-operative view;

HYPERTENSION OF RENAL ORIGIN AS OBSERVED AT OPERATION ON A SINGLE KIDNEY

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It is an exceedingly rare occurrence to operate upon both the kidney and the ureter in a patient having a single kidney. In recently operating upon such a patient certain observations were made which seemed to me to be of sufficient interest to record and which might be of value in the management of a similar case, should it be encountered.

CASE REPORT

An Italian Count, fifty-two years of age and married, was seen in consultation October 22, 1942. He gave a history that ten years previously the left kidney had been removed by Marion in Paris for what was said to be a renal papilloma. Following this, he was treated for a duodenal ulcer and under dietary restrictions and alkalies he had been comparatively comfortable. He had a tendency toward chronic constipation and took cathartics regularly. Five weeks before I saw him he had a chill which was followed by frequency and dysuria. There had been no hematuria. For twenty-four hours he had passed small amounts of urine at frequent intervals and with considerable discomfort. He was a man of large frame, weighing 205 pounds.

The general physical examination showed that most of the teeth had been extracted but there were several of doubtful vitality; the tongue was dry and coated; the heart and lungs were negative. There was tenderness in the right side of the abdomen and right lumbar region, but the kidney could not be palpated; there was a slight amount of abdominal distention; a scar was present in the left lumbar region. Reflexes were normal, blood pressure was 128/72. The external genitals were normal, the prostate congested and tender but not enlarged. He voided an ounce of concentrated urine which showed a trace of albumin, trace of sugar, excess of indican, urea 2.5 per cent, numerous pus cells, a small number of blood cells and numerous hyaline, epitheliated hyaline and finely granular casts. A Wassermann test was negative. An x-ray taken the following day showed a slight enlargement of the left kidney, the lower pole of which was palpable but not tender. Excretory urograms showed good function of the kidney, the dye outlining the ureter to the level of the ureterovesical junction, at which point there was an impacted calculus about 1 cm. by 0.5 cm. in size. There was no dilatation of the kidney pelvis or of the ureter.

Under increased fluids and following a colon irrigation, the urinary output increased and urinalysis showed only a trace of albumin, a small number of isolated pus cells, and a very small number of hyaline and finely granular casts. All pain, frequency and dysuria disappeared; however, anuria developed, and he had nausea and vomiting with pain in the right side of the abdomen and back. An attempt was made to pass a catheter to the right kidney but an obstruction was encountered

Fig. 1. Calculus impacted in pelvic ureter. Single kidney and ureter.

at a point 3.5 cm. from the bladder. No urine was seen coming from the right ureteral orifice. Following this manipulation the patient passed 5 ounces of urine but as he began to show uremic symptoms it was decided to do a nephrostomy.

Under cyclopropane anesthesia, the right kidney was exposed through a right oblique lumbar incision parallel to the lower border of the twelfth rib. Because of an excess of perirenal fat, the twelfth rib was resected and the kidney could then be drawn up into the wound with ease. The kidney was slightly enlarged and the cortex congested but otherwise appeared normal. The pelvis was distended and the wall slightly edematous. As soon as traction was made upon the kidney pedicle the anesthetist remarked that the blood pressure, which before operation was 120/58, was rapidly rising. I then applied pressure upon

the renal artery and the pressure readings registered 160/100 and 230/120. With the relief of pressure and all traction on the pedicle, the pressure subsided at once to 120/80. Pressure was again applied to the renal artery and the pressure rose to 220/120, then subsided to 160/120 and 150/110, but again rose under slight pressure upon the artery to 180/110, then subsided with the relief of the pressure to 130/90 and 120/70.

Fig. 2. Calculus impacted at ureterovesical junction.

The kidney pelvis was incised, a bougie was passed 28 cm. down the ureter at which point an obstruction was encountered which could not be passed. The renal pelvis was drained by a tube drawn through the cortex and middle calyx and sutured in a position which would completely drain the pelvis. The renal pelvis was then closed, sulfathiazole was applied freely, and the wound sutured in layers about the drainage tube.

The uremic symptoms disappeared rapidly under intravenous infusions of 5 per cent glucose, the urinary output became satisfactory and two days later the blood chemistry showed a reduction in urea nitrogen from 25 to 11.6 mg., the uric acid from 7.2 to 5.3 mg., the sugar was

118, CO_2 combining power was 44.3 vol. per cent and creatinin .95 mg. The blood count was normal, and the blood pressure remained within normal limits.

Under sulfadiazine therapy, the urine remained clear of infection. Trasentin was given at intervals and five attempts were made to extract the calculus in the lower right ureter by means of intra-ureteral manipulation. The calculus became engaged in the intravesical portion of the ureter but could not be withdrawn. Multiple catheters were passed

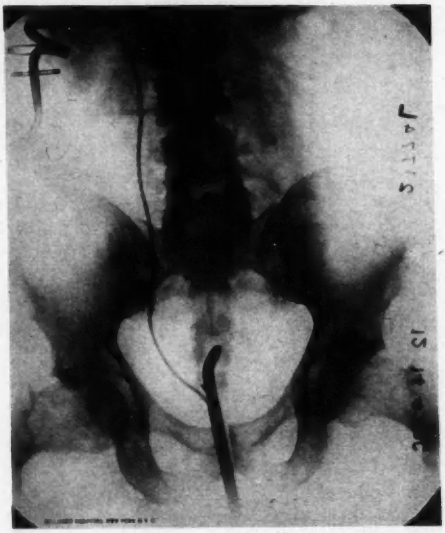

Fig. 3. Calculus pushed back to ureteropelvic junction.

and attempts made to engage the calculus. Catheters and bougies were allowed to remain in the ureter for twenty-four hours, the ureter was dilated and the Johnson basket was used, but all attempts failed to remove the stone. There was no reaction following any of these manipulations. The calculus could easily be pushed back to the ureteropelvic junction, showing that the ureter was dilated throughout its course above the bladder.

It was then decided to do a ureterolithotomy. The patient's general condition was excellent, kidney function normal with a blood urea nitrogen of 10.4 mg. and a uric acid of 4 mg. The diazine level was 5.4, blood count normal, blood pressure 120/72.

The question arose as to how one could be certain of retaining the

calculus in a fixed position in the ureter at the time of operation, the possibility of the calculus migrating up the ureter while the patient was in transit to the operating room being a serious one. I decided, therefore, to insert a Dourmashkin bag, push the calculus up to the brim of the pelvis, check with an x-ray, then inflate the bag thus fixing the calculus at this point. This procedure was followed; at operation the ureter was readily and satisfactorily exposed at the pelvic brim through

Fig. 4. Dourmashkin bag in position and distended, fixing calculus at level of pelvic brim. Note space between calculus and catheter caused by distention of bag.

a Gibson incision, the ureter opened through a longitudinal incision, 1.5 cm. in length, the calculus extracted and the ureter closed with one suture of 000 chromic gut. Sulfathiazole was dusted in the wound which was closed in layers about a small drain. The drain was removed in three days, there was no urinary drainage at any time and the wound was healed in seven days. The nephrostomy drainage was then withdrawn and no leakage took place from the kidney. This wound was healed in eight days. Urinary function became normal at once.

The postoperative course has been normal; the patient has had no urinary symptoms, the urine is clear and the blood pressure normal.

We are all familiar with various unilateral renal lesions as an etiologic factor in the production of hypertension, but rarely does

one have an opportunity such as was afforded in this case, of studying the direct and immediate effect upon the blood pressure due to interference with the arterial supply of a single kidney.

The use of the inflated Dourmashkin bag as a means of fixing a ureteral calculus at a desired point in the ureter, thus greatly facilitating its removal at operation is a method worthy of consideration. Such a method is especially valuable when doing a ureterolithotomy on a patient having a single ureter.

DISCUSSION

DR. J. DELLINGER BARNEY (Boston, Mass.): I was extremely interested in and admired the results of Dr. Balkus' ingenious presentation. I should like, in the first place, to ask for a little more detail about the wire which he uses. Is it steel piano wire, only of a very small size? All the steel piano wire I have seen is tough but very stiff, and if you once bend it, it will stay bent. It doesn't have the spring to it that you would like.

Many years ago some of my colleagues and I, using this same principle, made a self-retaining catheter from a soft rubber catheter by putting a thread through it and pulling it up. I am interested in seeing the same thing applied to the ureter. Perhaps Dr. Balkus has a specimen of the wire with him.

In regard to Dr. Davis' interesting presentation, it is discouraging to all of us people who have spent years on ingenious plastics on the ureter and kidney pelvis to have Dr. Davis show us how easily it is done in other ways. I think it is very illuminating. I wonder if Dr. Davis has tried the possibilities of dissolving the stone which remains with solution G. If the stone is phosphatic, it could easily be dissolved.

DR. LEON HERMAN (Philadelphia, Pa.): I have never permitted the use of rigid instruments in the ureter beyond the level of the intramural segment. To circumvent this Dr. Balkus devised the special catheter, which, I think, is the safest instrument for the purpose I have seen, but the use of which is certainly not devoid of danger.

I, personally, have used the instrument only once and that in the case of a pregnant woman whose ureter had been dilated twice and who had worn an indwelling ureteral catheter for twenty-four hours without success. The stone was removed with impressive ease by means of the modified catheter. The wire employed is No. 33 and is of stainless steel.

I still consider the use of rigid instruments in the ureter exceedingly dangerous and believe that very few of the tragic results of this procedure have reached the literature. Some time ago I saw a fatal generalized peritonitis case in the person of a boy eighteen

years of age, whose ureter had been ruptured instrumentally. I wonder how many unreported similar cases have occurred.

DR. EDWARD L. KEYES (New York, N. Y.): Dr. Davis, following the usual custom nowadays, believes in keeping the tube in the ureter a long time. I think it is two weeks.

DR. DAVIS: Thirty-one days was the longest.

DR. KEYES: In the ureter of my patient, reported by Dr. Davis, the tube was kept in for only three days, but it was a 20-F ureteral catheter. Possibly that is why the lumen of the ureter is still open twenty-eight years later, although the tube was left in so short a time. It seems to me the relation between size of tube and length or duration of intubation has not been worked out.

DR. YOUNG: Do you use that in other cases?

DR. KEYES: No, I use the T-tube a good deal. I have always cut a nick at the juncture of the T so the ends would fold back when it is pulled out.

DR. YOUNG: Do you object to leaving the tube in more than three days?

DR. KEYES: I don't object to anything, ever. I didn't know enough to leave the tube in more than three days, way back there in 1923.

DR. BARRINGER: Why does it keep open if you leave it three days; because the upper part is dilated? I don't understand the mechanics of it.

DR. KEYES: I don't, either.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): As the deviser of one of these metal instruments for manipulation of the stones in the ureter, I wish to second Dr. Herman in condemning the use of all metal instruments in the ureter. The instrument the doctor has brought before us is not without danger, though in his hands it has caused no injury. If, after more extensive use, no damage results, it may be added to our armamentarium.

I also wish to thank Dr. Bugbee for bringing out the point of using the Dourmashkin bag to fix the position of a stone in the

ureter. I have had the experience of playing hide and seek with a large stone that traveled up the ureter to the pelvis of the kidney. I exposed the lower portion of the ureter, and the stone immediately passed upward in the pelvis. I then exposed the pelvis, compressed the ureter below the stone, and removed it from the pelvis.

In regard to Dr. Keyes' observation about a ureteral stone passing after a nephrostomy, we have had a doctor who had a stone impacted in the lower ureter. It was about 1.5 to 2 centimeters in width. He had been to the Mayo Clinic, and they could not get a catheter beyond the stone, although they made repeated attempts. He had other doctors, and nobody had been able to get beyond that stone. Several months later he developed calculus anuria, with rigors and high temperature. We did a nephrostomy, because we could not pass any instrument beyond the stone in the ureter. That was about a year after the Mayos had treated him. It seemed that the stone was absolutely imbedded, so it could not be moved, and nothing could be passed beyond it. We did a nephrostomy on that man, and within two months after the nephrostomy was done the stone passed into the bladder. It is, therefore, a good thing to remember.

DR. C. RUTHERFORD O'CROWLEY (Newark, N. J.): I should like to cite a recent case of a stone in the lower ureter. This woman, twenty-one years old, married, came into my office about ten days ago. For the past five years she has been doctoring for stomach trouble, and three years ago her appendix was removed with no relief. She brought with her to the office, roentgenograms representing a gastro-intestinal series, and in one of these pictures I was able to see a stone in the lower third of the right ureter. Intravenous pyelograms were done on June 2, 1943.

The first flat plate showed this stone about the size of a small almond in the same position as before. The ten-minute pictures of both kidneys showed filling. Twenty-minute and thirty-minute pictures began to show slight dilatation above the stone. The last picture was a forty-minute picture in the erect position, and it showed very clearly the dilated ureter above the stone.

With a stone this size and in this position, it is better to have an open operation than any intra-manipulating in the ureter. It is going to do the patient less harm, with a better result, so that is what I am going to do as soon as I return home.

DR. WILLIAM C. QUINBY (Boston, Mass.): I wish to compliment the readers especially with regard to their ingenious progress in delivering stones, but more especially I wish to ask for further information from Dr. Bugbee about his most interesting patient. I address my remarks not to the stone factor but to the matter of this blood pressure phenomenon, because I feel that it is really a phenomenon, in a sense at least. I can't for the moment explain the hypertension which occurred, as I understand it, when you pulled on the renal pedicle or when you occluded the renal pedicle.

DR. BUGBEE: I pressed on the renal artery.

DR. QUINBY: The patient had but one kidney?

DR. BUGBEE: That is right.

DR. QUINBY: So far as we are able to determine physiologically, the blood pressure-raising factor in the kidney is entirely a humoral one. In other words, it is entirely independent of any nervous influence. Experiments have been done on this subject by various folks, among them myself, showing that, after the heart has been entirely denervated and all the sympathetics and adrenals removed, clamping of the renal pedicle causes the production in the kidney of a substance called renin which, when the clamp is released, immediately increases the blood pressure. These animal experiments, I think, are acknowledged to be sound, so, in animals in which the renal artery has been partially occluded, a persisting hypertension is caused because of the continuous presence of this substance, renin, in the blood stream.

Now, in the individual that Dr. Bugbee has told us about, the hypertension was caused on occlusion of the renal artery and disappeared when the occlusion was released. This is just the reverse of whatever we have thus far been able to find out from a physiological point of view. It seems likely that the rise in pressure which you describe might have been the same as that which would follow if you occluded the splenic artery, or if you occluded the aorta or any vessel of such size as to remove from the general circulation a certain amount of blood bed. The occlusion caused the remaining amount of blood to circulate through a smaller cubic space and, therefore, resulted in an immediate increase in systolic pressure which immediately dropped as soon as the occlusion was released.

That, to my mind, is an entirely separate and different affair from these conditions of hypertension caused by disease of the kidney of more or less long standing or in the acute experiments. I would, therefore, feel your experience was not the same as the instances in which a chronically existing hypertension is relieved by removal of the kidney. In other words, you were really not demonstrating the hypertension to be due to renal ischemia. It seems to me you were merely excluding a certain amount of the blood bed, or possibly stimulating the splanchnic nerve by traction. I can explain it in no other way.

I think you have made a very interesting observation, but I don't believe it falls in the same category with those in which we are interested today, in which hypertension is the result of unilateral renal disease.

DR. ARTHUR H. CROSBIE (Boston, Mass.): I would just like to bring out two very simple points regarding the removal of stones low down in the ureter through a median incision, that I learned from Dr. Vern Hunt years and years ago when he was at the Mayos.' They are both simple and undoubtedly all of you use them. The first one is the importance of a long incision. So many times I have seen a surgeon attempting to remove a low stone through a short incision. He always has terrific trouble. I don't hesitate to carry the incision up to the umbilicus and beyond it, if necessary.

The other is not to have too much distention of the bladder. If the bladder is distended too much, it overlies the stone and causes much more difficulty.

DR. MEREDITH F. CAMPBELL (New York, N. Y.): This past year I had an opportunity of making observations on two cases, which perhaps represent another phase of Dr. Bugbee's blood pressure observations. One of these was a four-year-old girl with an infected congenital hypoplastic or atrophic kidney with hypertension due to unilateral disease. Her blood pressure was 220/130 mm. Hg. The interesting observation was that at the time of pyelographic injection of the normal kidney, there was no alteration in the blood pressure. At the time of pyelographic injection of the diseased kidney, the systolic blood pressure jumped to 260, immediately dropping with release of the intrapelvic pressure.

An associate in the same hospital made identical observations in a forty-five-year-old man with systolic blood pressure of 210 mm. Hg., due to unilateral renal disease (chronic atrophic pyelonephritis). At the time of retrograde pyelographic injection of the diseased kidney, the blood pressure increased 40 points and dropped to the previous level with the release of the intrapelvic urographic tension. There was no change in blood pressure with distention of the pelvis of the good kidney. To us these observations suggested a possible diagnostic aid in the recognition of hypertension due to unilateral renal disease.

PRESIDENT RATHBUN: I think perhaps that is as far as we can go in this discussion in this limited time.

I will ask Dr. Wishard to close. (No closing remarks.)

Dr. Balkus!

DR. VINCENT BALKUS (Philadelphia, Pa.): In answer to Dr. Barney's question about the wire, I believe it is found in most operating rooms under the name of Babcock wire. It is very pliable and very strong and comes in very fine sizes, from 33 to 30, I believe.

DR. BARNEY: Isn't it only in Philadelphia that this is called Babcock wire?

DR. BALKUS: I think you are right.

DR. DAVID M. DAVIS (Philadelphia, Pa.): Dr. Barney asked whether or not we tried to dissolve the stone with solution G. We did not because I think this is a calcium oxalate stone. The urine has always been acid.

The last slides in my paper showed, I think, that the ureter in the operative area was really of normal size, or greater, at all points where it had formerly been so small. That narrowing extending over long distances interested me very much, because I have seen it before, extending through part or even all of the ureter. The entire ureter may be smaller than it should be, so that it might almost be called a micro-ureter or gracile ureter. It shows thus in retrograde or intravenous urograms. Perhaps it is an entity which somebody else can work out, and then we shall know more about it.

I have operated on a dog in connection with the intubated ureterotomy in an effort to obtain microscopic preparations of a regenerated ureter. A very strange thing happened. In order to get rid of

urinary drainage, I removed the kidney. I then slit the ureter and intubated it with a piece of No. 10 catheter. The dog did very well after this operation, just as do the patients. At the end of six weeks the animal was killed and autopsy performed, and, to my astonishment, the tube was gone. The dog had simply extruded this No. 10 tube through its tiny ureter and then through its urethra. On questioning the diener, I learned that about two and one-half weeks after the operation, some blood, apparently of urinary origin, had been seen on the floor of the cage. So that experiment was a failure, and we shall have to do it again before we can get good sections. However, the sections made from this dog showed that the ureter had healed, either before or after the extrusion of the tube, and that on the cut side of the ureter there was no muscularis. This evidence, then, is to the effect that the muscularis does not grow around the tube very promptly.

In reply to Dr. Keyes, I believe it is well to use as large a tube as possible. However, after the incision in the ureter is completed, one is limited in that respect by the size of tube which will go into the lower part of the ureter and still not be so tight as to cause ischemia of the ureteral wall, in which case sloughing will occur. We have found a No. 14 is the largest we can use in most cases and sometimes we have had to be satisfied with a No. 12.

Dr. Henry G. Bugbee (New York, N. Y.): Dr. Keyes said if the kidney had been drained for a period of time, the stone would have passed. The kidney was drained from October 31 until January 4, which is about nine weeks, and he had plenty of time to pass it. Not only did he have this period of nine weeks of drainage, but intra-ureteral manipulations were carried out during that time, and every attempt was made to relax the ureter by medication.

I did not attempt in any way to explain the rise in the blood pressure which took place when I applied pressure to the renal artery. It was just a coincidence that the anesthetist drew my attention to the fact that the pressure was going up very rapidly as I began to manipulate about the renal pelvis. Then I thought, "Well, the patient's condition is sufficiently good for me to do a little experimenting," so I spent ten or fifteen minutes experimenting and applying pressure and then releasing it. The rise in the pressure was so immediate and so dramatic that it seemed to me that the observation was worth recording.

I do not know whether similar pressure applied to a splenic artery would give the same rise in blood pressure, but there has been so much discussion about hypertension of renal origin that it seemed to me that these observations were worth recording.

DR. QUINBY: My objection is that it is not of renal origin necessarily, although it may be of renal origin.

LATERAL NON-RENAL RETROPERITONEAL NEOPLASMS

REPORT OF TWO CASES; CORTICAL CARCINOMA OF THE ADRENAL GLAND; PERINEURAL BLASTOMA

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Philadelphia, Pennsylvania

The majority of retroperitoneal extrarenal tumors are of adrenal gland, connective tissue, or lymphatic origin. In addition to the more common types, which originate from adult tissues, there is a small heterogenous group the origin and identity of which often confound surgeons and pathologists alike. These are generally believed to arise from vestiges of, or misplaced groups of cells occurring incidental to the complex development of the adrenal glands and urogenital organs. The mesonephros and gonadal structures undoubtedly give rise to many such neoplasms of which more than half are cystic. Totipotent germinal cells are the ascribed origin of teratomata and teratoid tumors of which Mecraig and Frazier collected thirty-six cases in 1937, but failed to include the case of an infant, aged six months, successfully operated upon by Campbell in 1933. The latter writer could find only four reported cases of totiblastic pararenal tumors. Non-renal hypernephromata, of which Barney reported a collected series of thirteen cases in 1937, are believed to originate from accessory groups of adrenal cortical cells.

Detailed description of rare tumors is desirable as the means of accumulating clinical and pathological data, for which reason, we wish to present two rather extraordinary cases.

CASE REPORTS

Case 1.—Perivascular carcinoma of the cortex of the left adrenal gland. V. D., an Italian tailor, aged thirty-seven, was admitted to the medical wards of the Pennsylvania Hospital on March 2, 1936, complaining of bulging of the lower left chest and adjacent portion of the abdomen. Examination disclosed a large mass in the upper left abdomen. Urography showed that the left kidney had been displaced downward and rotated, and indented by the overlying tumor.

Having refused further examination, the patient was discharged with the tentative diagnosis of renal neoplasm.

The patient was sent to the urological department on May 19, 1937,

where we first saw him. He was symptom free, apparently in good health and with normal blood pressure. The temperature and pulse and respiratory rates were normal. We noted marked bulging of the upper left abdomen with flaring of the lower left chest wall. Palpation disclosed a large, smooth mass occupying the major portion of the left side of the abdomen and extending upward beneath the costal margin. This was quite firm and moved with respiration. It was neither tender nor pulsating, seemed to extend into and fill the loin, and measured approximately 27 cm. in its vertical diameter. There seemed to be a more or less distinct mass at the lowermost portion of the main tumor which was thought to be a displaced kidney. The upper border of dullness reached as high as the sixth rib in the anterior axillary line and to within 3 cm. of the angle of the left scapula. The lower border was a finger's breadth above the iliac crest. That the mass had increased in size from March, 1936, was evident from comparison of roentgenograms made on the first and present admissions; the psoas shadow was now obliterated, the heart had now become displaced and was in a rather horizontal position, and the stomach and intestines were further displaced.

Laboratory studies disclosed normal renal function (phthalein output, 70 per cent; blood area nitrogen, 13.7 mg. per cent), and normality of the blood. There were no demonstrable pulmonary or skeletal metastases. A retrograde pyelogram reproduced the changes noted in secretory urograms made one year previously. Dr. Bishop remarked: "The appearance of the retrograde pyelogram, which suggests downward displacement and compression of the kidney by an extrarenal mass rather than by a mass within the kidney, is much the same as shown in secretory urograms in 1936."

The right kidney excreted 27.5 per cent phthalein, the left one 17 per cent in a fifteen-minute period. The pre-operative diagnosis was "lateral retroperitoneal extrarenal neoplasm; origin and type unknown."

On May 28, 1937, under spinal anesthesia, a very large, smooth, well encapsulated, movable extraperitoneal mass was exposed through the usual loin incision. After partial mobilization the mass was found to be attached to, but probably not originating from the kidney. However, tumor and kidney were mobilized together, the former extending far upward beneath the diaphragm. The only technical difficulty encountered was in delivering the large mass. Ligation of the renal pedicle controlled all bleeding, the neoplasm being vascularized by branches from the renal artery. Convalescence was uneventful.

The specimen consisted of a large, soft, smooth, encapsulated, ovoid mass measuring 27 by 17 by 11 cm. with somewhat compressed, but otherwise normal appearing kidney attached to one end. The weight of the mass was 3180 gm. (7 pounds). On section (Fig. 1) the cut surface around the periphery consisted of a thick capsule beneath which the tissue was very soft and spongy. It was yellowish orange with

many small hemorrhagic areas. This tissue, which had an average thickness of 3.5 cm., extended all around the periphery and was separated into large lobules by fibrous fasiculi. Beneath this layer, the center or medullary portion consisted of yellowish, hyalin, translucent, gelatin-like material with many islands of yellowish, soft, spongy, opaque tissue, the central portions of which were very friable. The kidney had been

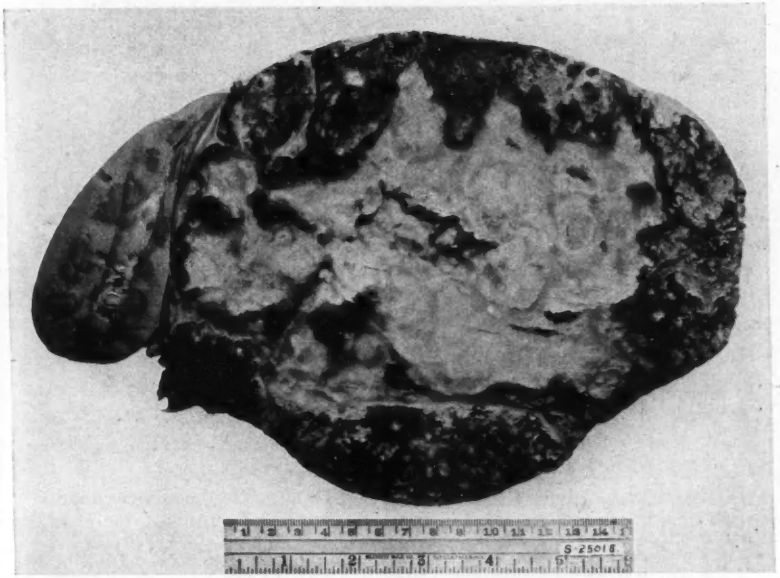

Fig. 1. Sectioned surface of neoplasm and kidney in Case 1.

compressed at one point by the neoplasm but otherwise showed no gross changes. The kidney and neoplasm were separated by the capsule of the latter and the renal capsule; and there was no evidence that the neoplasm was of renal origin.

Microscopically (Fig. 2), the entire center of the mass was necrotic. At its periphery, however, scattered groups of cells were well preserved. These were often arranged around large vascular channels which are lined with single layers of endothelium. The cells had no definite alveolar arrangement and were grouped in sheets which often resembled islands in the blood channels. The cytoplasm was abundant and pink staining, but the cells varied widely in size and shape. Most of the nuclei were irregular and hyperchromatic and contained prominent nuclei. Multinucleated giant cells were numerous. Although the cells

were moderately anaplastic, they distinctly resembled the fasicular cells of the adrenal cortex and appeared to be malignant. The broad sheets of polygonal foamy cells characteristic of hypernephroma were lacking. The kidney was normal. Diagnosis: "Perivascular carcinoma of the cortex of the left adrenal gland; normal left kidney." (R. F. Norris.)

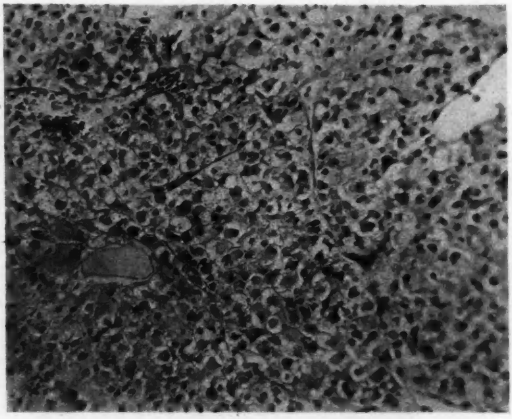

Fig. 2. Microphotograph of neoplasm in Case 1.

The patient returned January 10, 1941. He had been complaining recently of intermittent pain in the left groin, left lumbar region and chest. For two weeks prior to admission, there had been persistent pain at the level of the twelfth rib in the midaxillary line. Tenderness and the suggestion of crepitus over the rib led to the tentative diagnosis of pathological fracture which roentgenography failed to disclose.

Despite deep roentgen therapy for suspected involvement (metastatic) of the twelfth rib, the pain increased becoming so severe that the patient was totally incapacitated. After six weeks confinement to bed at home he returned to the wards on April 20, 1942. There had been marked loss of weight. The body was markedly and rigidly bent toward the left as the result of scoliosis of the dorsolumbar spine, and the patient was obviously in great distress. Neurological examination by Dr. Alpers disclosed evidence of disease of the lumbosacral plexus and of nerve roots from T 5 to L 2 inclusive, the former being due in all probability to carcinomatous involvement, the latter more likely to toxic radiculitis.

Choice of treatment lay between x-ray therapy, together with rhizotomy (T 8 to L 1 inclusive), and cervical cordotomy. The latter oper-

ation was performed by Dr. Francis Grant with complete relief of the pain and associated muscular spasms leading to scoliosis. The patient had gained in weight and strength and had returned to work. General physical examination disclosed no evidence of recurrence of the neoplasm. Dr. Alpers reported negative findings in a neurological reexamination on February 1, 1943,

Comment.—The source of the tumor in this case remains undetermined. Its structure suggests that it originated either from normally situated or accessory adrenal cortical tissue. I know of no positive proof that neoplasms arising from misplaced cortical cells are associated with endocrine changes. Prepubescent males with cortical adrenal neoplasms are much more likely to show endocrine disturbances than adult males with identical tumors. These changes express themselves in the form of true or homologous puberty, in contrast to the heterologous type commonly found in prepubescent girls with similar neoplasms.

Player and Lisser, in 1933, added a case to eight authenticated cases found in the literature up to 1932. Their case, the first to survive adrenalectomy up to that time, was that of a boy aged four years and eleven months whose extraordinary sexual development was first noted between the ages of one and one-half and two years. His general appearance was that of a boy seven or eight years of age; his bone age was between eleven and twelve years, but he was not of the Herculean type. The prostate gland was of adult size and spermatozoa were found in the vesicular contents. Erections and emissions occurred frequently. Retrograde pyelography disclosed downward displacement of the left kidney with flattening of the upper major calyx, due to a rounded tumor mass at the upper pole of the left kidney. The tumor proved to be an adrenal adenoma that weighed 278 gm. and measuring 7.5 by 9 cm. Comparatively little improvement was noted in the endocrine abnormalities twenty months after operation.

A case quoted by the same authors illustrates the excessively rare feminizing characteristics due to adrenal cortical neoplasms in the adult male. The case described by Holl was that of a male school teacher forty-four years of age who was a father and had been sexually and otherwise normal until two years before operation when feminization began and slowly progressed. This was characterized by loss of libido, impotency, obesity, atrophy of the genitals, partial loss of hair and gynecomastia. Complete restoration

of male characteristics occurred within several months, after removal of an adrenal neoplasm. This case seems to be a rare exception to the rule, namely, that in adult males cortical adrenal neoplasms, as in our case, grow slowly, often to great size in the complete absence of endocrine disturbances. In this event, the nearest approach to a correct diagnosis in the majority of instances is that of lateral, extrarenal, retroperitoneal neoplasm.

Case 2.—Pararenal perineural fibroblastoma. R. B., a negro laborer, aged fifty, was admitted to the urological service in the Pennsylvania Hospital on September 15, 1942, complaining of pain in the left upper abdomen and a "lump" in this area. Five months or more prior to admission, the patient noticed a "lump" in the upper left abdomen. This was painless and had not increased in size until three and one-half weeks before admission when while lifting some heavy lumber, he injured the involved side since when there has been pain and tenderness in this region, and the lump has increased in size. He continued to work, however, until the day before admission when the pain suddenly became quite severe. This, in all probability, was due to intratumoral hemorrhage. The discomfort was aggravated by motion and deep breathing. There was no history of chills, sweating or fever, but the patient had lost weight, possibly 10 pounds in the last month. There was no history of symptoms suggestive of urogenital, pulmonary, or cardiac disease except as already noted. He had pneumonia some years ago, syphilis in 1936 with inadequate treatment, and suspected pulmonary tuberculosis in 1935.

General physical examination was essentially negative except for evidence of undernourishment and extensive dental caries and mouth infection. There was considerable bulging of the upper left abdomen with overlying rigidity of the muscles and considerable tenderness. Palpation disclosed a large, hard, irregular, apparently fixed mass which extended beyond the midline in the epigastric region and to a point several centimeters below the level of the umbilicus. In the epigastric region, several large dense nodules bulged the abdominal wall, and the main portion of the tumor extended into the renal area. However, it was our first impression that the tumor was of intraperitoneal origin. The external genitalia and prostate gland were normal. There was no evidence of endocrine disturbance.

Laboratory studies were essentially normal; there was no urinary infection and the routine blood, renal function and serological tests were normal.

Cystoscopy yielded no diagnostic data of value, although the left kidney function was slightly diminished. Retrograde pyelography disclosed downward and medial displacement of the left kidney with peculiar distortion of the pelvis and calyces (Fig. 3) but with only

slight redundancy of the ureter. Interpretation of the bizarre elongation, curvature and overlapping of the calyces proved difficult and, as events proved, erroneous. It was our impression that the abnormality was of developmental rather than of acquired origin.

An intravenous urogram showed satisfactory excretion of the dye on both sides. The right kidney was apparently normal. The left kidney

Fig. 3. Pyelogram in Case 2 showing downward displacement with distortion. Compare this with the postoperative pyelogram (Fig. 6).

was in the same position and the urographic shadow presented much the same appearance as in the retrograde pyelogram. It was the opinion of the roentgenologist (Dr. Bishop) that the x-ray evidence indicated the presence of an extrarenal neoplasm while the apparent absence of ureteral redundancy suggested congenital renal ectopia. There was no evidence of pulmonary or skeletal metastasis.

Pre-operative diagnosis: Lateral, extrarenal retroperitoneal neoplasm of undetermined origin and type.

On September 15, 1942, under spinal anesthesia, an upper left rectus muscle splitting incision disclosed an enormous retroperitoneal neoplasm. The tumor was somewhat movable, seemed to be quite solid, and was regularly smooth and ovoid in contour except at its upper inner portion where there were several large nodules. The omental veins were enormously distended, but there were no metastatic nodules to be found and no ascites. The displaced left kidney was freely movable and without any attachment to the tumor mass. After incising the posterior layer of the peritoneum and displacing the large gut medially, mobilization of the tumor was begun laterally. The mass was in the main, solid and heavy, but obviously composed of solid, yellowish, white tissue and blood filled cysts. Despite considerable hemorrhage, mobilization proceeded without difficulty until the anterior medial surface of the mass was reached at which point the stomach was densely adherent. In attempting to separate the latter from the mass by sharp dissection, both structures were opened, the tumor yielding a considerable quantity of dark brown fluid. The opening in the stomach was immediately repaired after which mobilization of the tumor was completed. Various vessels of supply were easily identified and ligated, and the tumor removed without further difficulty. Two rubber covered drains were placed in the tumor bed and the wound closed.

Convalescence was uneventful until September 18, 1942, when the patient became dyspnoeic as the result of slight transient pulmonary edema. On September 24, 1942, mild, intermittent colicky abdominal pain followed by vomiting occurred. Our suspicions of partial high intestinal obstruction were confirmed on September 26, 1942, when Dr. Walkling freed a knuckle of jejunum which had become adherent at the site of the incision. The subsequent course was uneventful, and the patient was discharged in good condition. Reëxamination on May 1, 1943, showed no recurrence of the neoplasm. The patient had gained 15 pounds in weight and was in good health.

Dr. John Bauer described the neoplasm as follows: "Specimen consists of a large tumor mass measuring 22 by 15 by 12 cm. The mass which weighs almost 12 pounds, comprised 1220 gm. (2.5 pounds) of neoplastic tissue, the remainder being fluid and clotted blood. The mass is surrounded by a capsule covered with fibrous tags. The mass is soft and lobulated."

On section (Fig. 4), the cut surfaces showed numerous cystic spaces having smooth thin walls. The cysts contained finely granular particles grouped in masses which were chocolate in color. Some of the cysts which contained clotted blood were small, while others were large. The tumor mass in other parts had a gray-white stroma and was uniform in structure. It was soft and cut easily.

The microscopic appearance of the tumor (Fig. 5) was rather dis-

Fig. 4. Sectioned surface of neoplasm in Case 2.

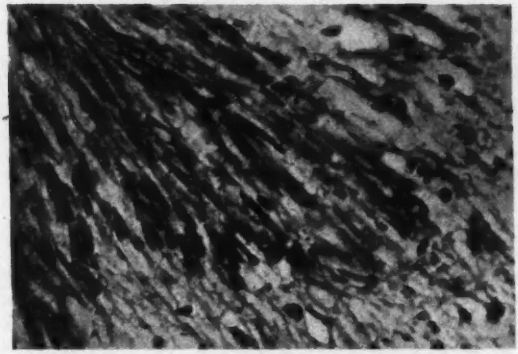

Fig. 5. Microphotograph of neoplasm in Case 2.

tinctive. There were many irregular whorls of closely packed elongated, narrow spindle-shaped cells, with long narrow deeply-stained vesicular nuclei. The nuclei were grouped more or less in parallel bundles or sheaves (so-called Verocay bodies). The cytoplasm was vesicular in places, suggesting previous deposits of lipoids. With Mallory's modification of Heidenhain's azo-carmine stain, the nuclei of these cells

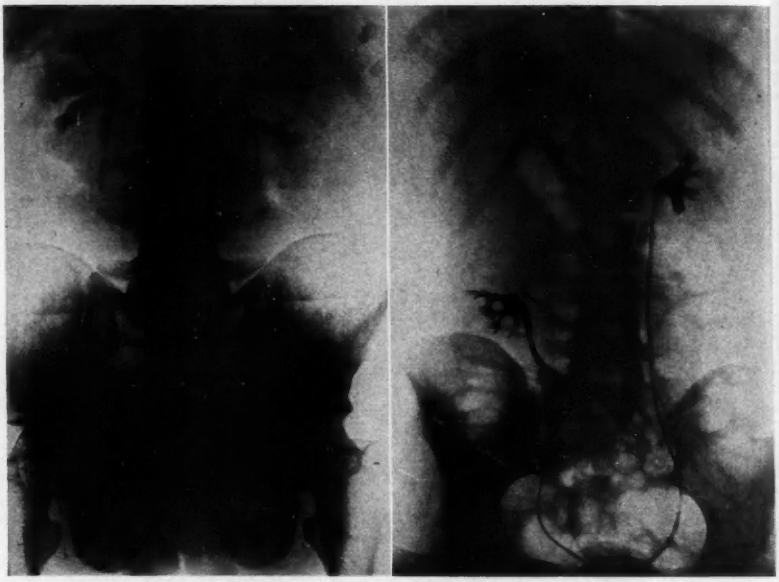

Fig. 6. (*left*) Postoperative pyelogram in Case 2.

Fig. 7. (*right*) Pyelogram in a case of pyonephrosis (closed) involving the upper half of a double kidney and simulating to physical examination an extrarenal neoplasm.

were distinctly red. The cytoplasm was ill defined, but throughout were thin straight or slightly wavy filaments, which formed a reticular network, that in places became homogenous in broad bands. This collagenous reticulum was abundant throughout and seemed to be the product of the spindle-shaped cells. With light green modification of Masson's trichome stain the nuclei were reddish black. The cytoplasm was somewhat granular, of a hue similar to that of the nuclei, interspersed with pale, ill defined, green staining fibrils. No nerve cells were present. There was nothing in the mass, grossly or microscopically to vaguely resemble either kidney or suprarenal gland. The appearance suggested

an origin from fibrous tissue about nerve fibers, and in this respect it closely resembled the so-called schwannoma. It was much larger than those usually described, however, but like them was featured by cysts and necrotic areas. Diagnosis: Perineural fibroblastoma (retroperitoneal region).

Comment.—Peripheral neoplasms of the type described above are

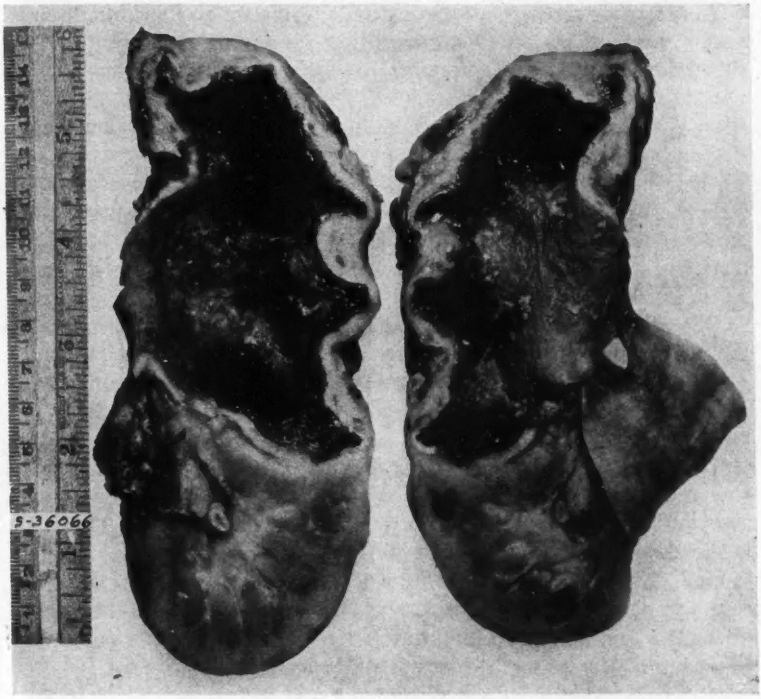

Fig. 8. Photograph showing pyonephrosis in upper segment of a double kidney (see Fig. 7).

believed by the majority of pathologists to originate from Schwannian syncytium, a neurectodermal structure. The controversial phases of this intricate subject were discussed by P. Masson in 1932 in an exhaustive study of experimental and spontaneous peripheral nerve tumors.

The neurogenic neoplasm in our case is unusual in size and loca-

tion and its exact point of origin undemonstrable. There is no reason to suspect that it originated from the medulla of the adrenal gland. Notwithstanding the retroperitoneal position of the tumor, the associated renal distortion and misplacement were thought to be of developmental origin. A postoperative pyelogram (Fig. 6) shows that the kidney has ascended to the normal position and that the pelvis is bifid, the latter together with rotation of the kidney and partial ureteral obstruction, accounting for the pre-operative pelvic distortion (Fig. 3). Differentiation between renal and nonrenal masses causing renal displacement, without marked renal destruction, is most difficult. There are, however, two renal lesions that demand serious consideration; namely, simple serous cysts, and distention due to ureteral occlusion of one segment of a double kidney. The large, simple cyst variously displaces the kidney and causes some, usually slight loss of function incident to pressure atrophy; its differentiation from extrarenal neoplasms or cysts may be impossible.

Recently we found a large, rounded, nontender movable mass in the right renal area of a thin, anemic girl, aged sixteen. The urine contained a few pus cells and the bladder was chronically inflamed. The temperature and leukocyte count were normal. The kidney, which was normal in function, was displaced downward; the pelvic outline essentially normal (Fig. 7). The pre-operative diagnosis was retroperitoneal, nonrenal neoplasm, probably lymphosarcoma associated with mild urinary infection. Exploration disclosed a large closed pyonephrosis involving the upper half of a double kidney (Fig. 8). Selection of the transperitoneal approach in our case of neurogenic neoplasm was fortunate, since its removal through a loin incision would have been difficult, if not impossible. Drainage of the tumor bed through a counter-incision in the loin is usually preferable to anterior drainage and in the present instance might have prevented postoperative obstruction. We rarely use the transperitoneal approach in the case of primary renal neoplasms except in young children.

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RETROPERITONEAL TUMORS

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All enlargements of the kidneys are considered retroperitoneal tumors. I am including one case of calculous pyonephrosis in this study because of the unusual renal reaction to transfusion.

Braasch, in the preface of the first edition of his epoch-making book *Pyelography,* said that he hoped the book "may increase the value of the method and permit the more general usage which it deserves." His modest request has grown to the exact diagnosis which modern urology expects of the urologist. However, many urographic studies are indeterminate until operative or autopsy material is available.

Too many surgeons, while able technicians, require no more than the knowledge that the case is for operation or not. We are critical of our pre-operative diagnosis.

The diagnosis of retroperitoneal tumors, however, is by exclusion. Complete physical and roentgenological study of the urinary and gastrointestinal tract must be done.

Of the retroperitoneal growths the kidney is the most frequently involved organ with disease or tumor enlargement and must first be considered as the origin of the tumor. Besides the kidney the tumor may be derived from the adrenal gland or the parietal tissue.

I am not considering tumors of the kidney as they have been so completely studied by many authorities.

Tumors of the adrenal gland may arise from the connective tissue. The most common of the cortical tumors are adenoma, carcinoma and rarely melanoma. The tumors from the medullary portion are relatively rare. The most interesting are the sympathoblastoma derived from nerve tissue and the pheochromocytomata.

The parietal tumors arise from connective, lymphatic fat and, as in the case reported, from nerve tissue.

CASE REPORTS

Case 1.—Neurogenic sarcoma. E. B., aged fifty-two, married, was admitted to St. Luke's Hospital March 10, 1943. Six months prior to admission she noticed a mass in the left abdomen which grew progres-

sively larger. Four months before admission she had pain in the left abdomen radiating to the midline. During this time she was comfortable only when lying on her left side. She had no urinary symptoms. Since onset of illness she had a weight loss of 30 pounds. Right nephropexy and appendectomy were done in 1911. The remainder of her history is irrelevelant.

Physical examination was negative except for a mass completely filling the left half of the abdomen. This was variously diagnosed by the internist as splenomegaly, by the surgeon as renal tumor, and was thought to be adrenal by me. The blood pressure was 140/70.

Laboratory Studies: Hemoglobin 88 per cent, red blood cells 4,200,000, white blood cells 13,900, 80 per cent polymorphonuclear cells.

Cystoscopic examination revealed a normal bladder. Catheters went readily to both kidneys. Indigo carmine appeared in good concentration in three minutes from the right and four minutes from the left kidney. Examination of the separate urines was negative.

X-rays: Left upper quadrant tumor, probably renal or adrenal; left hydronephrosis with normal architecture. Chest x-ray: No evidence of metastases; diaphragm elevated on left side.

On March 18, through the transperitoneal approach, a transverse incision was made first, and the mass was immediately under the incision. All the abdominal viscera were displaced downward and medially. The kidney appeared to be intimately attached to the tumor as no definite line of cleavage could be found. After ligating the renal vessels and separating the ureter the tumor was dissected free. There was a definite capsule with none of the dilated vessels usually associated with a renal tumor.

The fourteenth day after operation the patient went into shock with pallor, drop in blood pressure to 70 systolic and rapid pulse. She complained of pain in the right upper abdomen, and a small mass could be felt in the liver. This episode lasted only one hour, and from then on her convalescence was uneventful. She was discharged on her twenty-first postoperative day.

Pathological Diagnosis: Neurogenic retroperitoneal sarcoma; normal left kidney. The specimen weighed 3150 gm. with attached left kidney and adrenal. The tumor was a lobulated mass 21 by 17 by 10 cm. One-half of the surface was covered by a smooth, pale peritoneum showing adherent fat at several points and some areas of congestion. On section the tumor was made up of lobules which contained pale, homogenous, gelatinous tissue. These lobules varied in size from 3 to 5 cm., and at some points there were areas of yellow degeneration. The capsule of the kidney stripped readily. At one point there was a cyst 6 cm. in size filled with clear fluid. There was a strip of adrenal tissue 8 by 2.5 by 0.5 cm.

Microscopic slides from various positions showed essentially the same picture, the tumor being composed of derivatives of the neurillemma, the nuclei varying according to the amount of edema present.

Some of them were large, but rather widely separated, but most of them formed a fine network with parallel strands of elongated cells. In some areas these had the twisted appearance of nerve bundles, and multinucleated cells resembling ganglion cells were sometimes found. There were numerous atypical mitoses, and the tumor was a malignant one which may be expected to recur. The portion of adrenal appeared normal.

In this case, as in the one described by Sailer, there were no tumors of the Von Recklinghausen type and, as pointed out by Frank, metastases are less common than local recurrence. According to the latter, metastases occur not more frequently than 13 per cent. Surgery is conceded to be the only type of therapy that is successful despite the one patient treated by Adair, who responded to x-ray therapy and was well two and one-half years afterward. Ransom and Kay say retroperitoneal tumors are not rare and are usually benign. Rasmusson found nine retroperitoneal tumors in 42,000 patients while Gurlt found only one retroperitoneal sarcoma in 899 cases of this disease.

Judd and Larson reported only one case of neurogenic sarcoma—paraganglioma—which developed in the suprarenal gland.

The histogenesis of these tumors is controversial. Virchow called them false neuromata. Verocay thought them to be ectodermal in origin, arising from the sheath of Schwann and called them schwannomas. The presence of a capsule suggests an origin from neurofibromatous structure.

Case 2.—Adrenal carcinoma. A. F., aged forty-seven, an unmarried woman, was admitted to the hospital, July 29, 1942. Her chief complaint was pain in the spine and left lumbar region, especially when she walked or stood. Neurological and orthopedic examinations were negative. She had a weight loss of 40 pounds in the four weeks in which she noted these symptoms.

Physical examination showed an acutely ill woman with pallor and a palpable mass in the left upper abdomen. The blood pressure was 124/76.

Intravenous pyelograms July 30, 1942 showed a normal right pelvic outline but distorsion and flattened renal pelvis on the left. The chest showed several small and medium-sized, round patches of increased density, having a cotton-ball appearance typical of pulmonary metastases. There was no evidence in the bones of any metastatic involvement.

The tumor was removed August 3, 1942, through a lumbar incision with removal of the twelfth rib. The tumor and kidney were united

by some strands at the upper pole of the tumor. The kidney was sacrificed. Despite the evident lung metastases, it was hoped they might later respond to deep x-ray therapy.

The patient had two transfusions following operation. Her urinary output was 90 c.c. on the first postoperative day, 20 c.c. on the second postoperative day, 225 c.c. on the third and 510 c.c. on the fourth. For the first three days her blood pressure remained below 70 mm. systolic until she was given 10 mg. of desoxycortico steroneacetate on the second and third postoperative days. With the rise in blood pressure, her urinary output increased.

Her postoperative course was hectic as an almost immediate metastatic lesion developed in her liver. She also had two attacks of infectious parotitis.

The patient was discharged from the hospital on October 4, 1942 but was readmitted November 29, 1942. There was a gradual increasing nitrogenous retention in blood and a diminishing amount of urinary output, resulting in death.

Pathological Diagnosis: Carcinoma of adrenal cortex, left; congestion of kidney, left. The kidney was 12 cm. long and 7 by 5 cm. at the hilum. Attached to the upper pole there was a lobulated mass 14 by 10 cm. covered with a thin, semi-translucent capsule. The tumor was composed for the most part of soft yellow tissue, mottled, with areas of hemorrhage. Most of the tissue was soft and friable.

Microscopic examination of sections showed relatively normal kidney but with many of the tubules filled with a coagulum and some desquamation and atrophy of the tubular epithelium.

Sections of the tumor showed a growth which was derived from the cortical cells of the adrenal which were growing in large sheets, tending to palisade around large veins and dilated capillaries. The cytoplasm was somewhat vacuolated or stippled in appearance, and fat stains showed that there was a fairly large amount of lipoid in many of them. Some, however, were fairly free of it. The fat was very finely divided and was found only in large masses where the cells had broken down and lipoid material had been extruded. The nuclei were in general rather small and oval, but some giant and even multinucleated forms were present. A few mitoses were found throughout. At the periphery, where the tumor was very hemorrhagic, masses of it were growing freely in the tissues and the growth was evidently invading. It had the appearance of a malignant growth arising from the zona fasiculata of the adrenal cortex. Tumors of this type metastasize usually to nodes and lung by the blood stream and less frequently to bones than do the hypernephromas of the kidney.

Case 3.—Calculous pyonephrosis. The surgery of the kidney has been well-outlined through the years.

A fifty-four-year-old woman was admitted to Woman's Hospital for the repair of her pelvic outlet resulting from three normal deliveries. Following this operation, it seemed advisable to give her a transfusion

for a slight secondary anemia. She was given 500 c.c. of citrated blood on April 21, 1942, and again on April 23, 1942, with a slight febrile reaction after each one. On April 30 she was given 500 c.c. more. This was followed by a chill and rise in temperature to 104 F. A progressive oliguria ensued, indicating renal damage. She was actutely ill, her urea nitrogen rose to 74 mg. and her CO_2 combining power dropped to 22. With parenteral fluids including sodium lactate, she recovered from this reaction but still had an elevation of temperature, and pain and a mass developed in the left upper quadrant. X-ray showed a staghorn stone in the kidney on that side. This kidney was subsequently removed.

The interesting feature in this case is the reaction following the first three transfusions. A check of the blood showed the patient's blood to have a negative Rh. factor. All the donors had Rh. positive blood. Two subsequent transfusions failed to cause reactions when Rh. negative donors were used.

The obstetricians are familiar with this reaction in the prevention of erythroblastosis. My plea is to determine the Rh. factor in all transfusions in order to avoid these reactions which cause a considerable degree of morbidity because of the iso-immunization that results from blood not properly matched.

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LYMPHOSARCOMA OF THE URINARY BLADDER

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Lymphosarcomatous tumors of the urinary bladder are rare. Only five cases have been previously reported. The first two cases were presented simultaneously by Eve and by Chaffey before the London Pathological Society in 1885. They were published in its transactions. Both presentations were postmortem specimens. Eve's specimen was the right half of a bladder removed from a man aged sixty-eight. The patient had suffered from pain in the loins for several years and died in 1883. The pelves of both kidneys and the ureters were dilated. The bladder tumor was very large and occupied most of its wall. Its greatest thickness was 3½ inches. On the outer side of the anterior wall a round nodule had grown the substance of which was continuous with that of the prostate. The histological examination showed the tumor to consist of round lymphlike cells with a varying amount of fibrous stroma. There are two sketches by the author.

Chaffey's case was that of a boy three years old who had had urinary difficulties since the age of eight months. Four days before admission to the hospital complete urinary retention had set in, but only small amounts of urine could be drawn off with the catheter. A perineal section was performed and seven days later the child died. The autopsy description is limited to the bladder which contained a large nodular tumor on the anterior wall and on the trigone. The growth consisted of a fibrillar network containing in its meshes lymphoid cells. In some portions the fibrillar elements appeared to be absent, the growth being composed entirely of round and spindle cells. There are no illustrations.

The third case was reported by Maragna in 1927. The tumor occurred in a man thirty-seven years of age who had suffered for many years from frequency, dysuria and hematuria. Cystoscopy showed a large mulberry-shaped calculus and a chestnut-sized tumor on the posterior bladder wall. The urine contained blood and pus. The stone and the tumor were removed by suprapubic cystotomy. The patient left the hospital but died eight months later with a large

mass in his pelvis and a huge liver. The sections showed masses of small lymphocytic cells in a fine stroma and the tumor cells had invaded the various layers of the bladder wall. There are no illustrations. The author discusses at length the normal histology of the human bladder which does not contain lymphatic tissue and comes

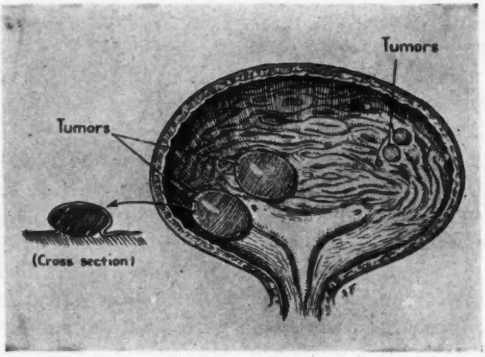

Fig. 1. Sketch of bladder.

to the conclusion that a lymphosarcoma of the bladder must necessarily be preceded by chronic infection and lymphatic tissue proliferation.

The fourth case was reported by Dupont and Misrachi in 1931. Their patient was a woman thirty-two years of age who had suffered from urinary frequency and dysuria for seven months. Hematuria had been present intermittently and the urine was found to be infected. On operation two tumors were found. One, which was white, smooth and round, was located on the bladder floor close to the internal meatus; the other, which was irregular in shape, reddish and ulcerated, grew on the right lateral wall. Both tumors were resected and the patient made an uneventful recovery. Eight months later the follow-up showed no recurrence. The histological picture was that of an invasive growth consisting of reticulum cells and lymphocytes invading the muscularis. In many of the sections the mucosa had disappeared.

Kreutzmann reported the fifth case in 1942. The patient was a woman forty-seven years old who gave a history of recurrent bouts

of cystitis for twenty-five years. Intermittent hematuria had been observed for three years. The urine was infected. Cystoscopic examination showed a smooth round mass on the posterior bladder wall. A complete resection of the tumor-bearing area was carried out and mild roentgen ray therapy (450 r) was used. No recur-

Fig. 2. Lymphosarcoma of bladder. (Low power)

rence was found twenty months after operation. The histological sections showed a mixture of small and large round cells infiltrating the muscularis and disappearance of the mucosa. The stroma was scanty and the tumor was not sharply limited. There are two illustrations.

Our case is that of a woman sixty-four years old with a ten years' history of recurrent cystitis. There had been marked frequency off and on but no hematuria. Her laboratory workup showed a normal blood count, a negative Wassermann test, and numerous pus cells in the urine, which yielded B. coli on culture. Cystoscopy on October 13, 1942, showed two round sessile tumors in the region of the right ureteral orifice and two small ones on the left lateral wall well above the left ureteral orifice. The larger tumors looked like young mushrooms, perfectly smooth, white and slightly recessed at the level of the bladder wall; the smaller ones looked like half-buried peas. All of them were

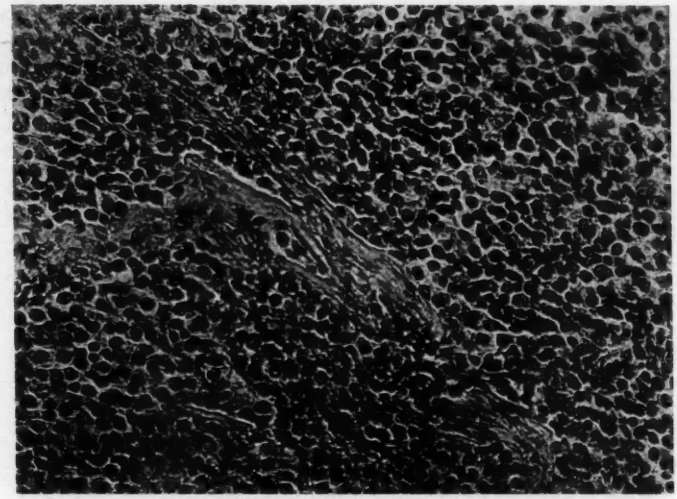

Fig. 3. Lymphosarcoma of bladder. (High power)

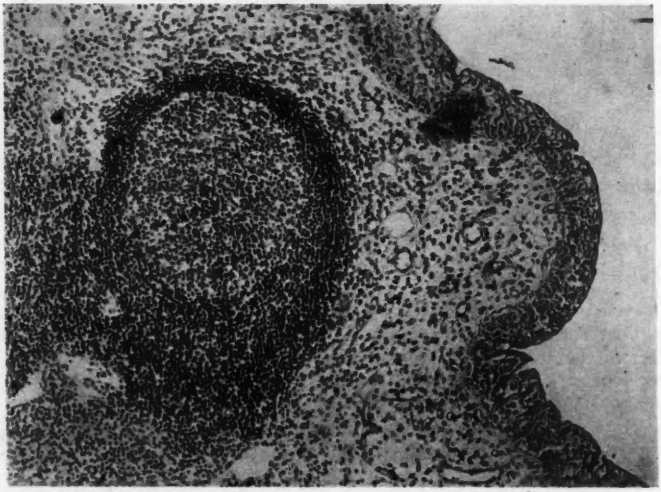

Fig. 4. Small lymph follicles in bladder.

covered with intact bladder mucosa. A small piece was pinched off one of the larger tumors for histological diagnosis. On October 20, 1942, the bladder was opened. Two tumors of 2.5 cm. in diameter each were found in the region of the right ureteral orifice and three pea-sized tumors were found on the left lateral wall (Fig. 1). A complete resection was impossible without transplanting the right ureter and the general condition of the patient excluded such an extensive procedure. Therefore the tumors were excised as completely as possible with a loop and the bases fulgurated with the coagulating current. The bladder was closed and an indwelling catheter was placed. Recovery was uneventful.

Postoperative treatment consisted of 4100 r of roentgen ray through five portals.

Six months later cystoscopic examination did not show any recurrence.

Grossly the tumors consisted of firm, white, elastic, rubberlike tissue. They were sharply defined, covered with intact mucosa, and did not infiltrate into the muscularis. Histologically (Dr. Arnold de Veer) the tumors present the general picture of lymphoid tissue consisting of two different types of structure (Figs. 2 and 3). The predominant one resembles that of germinal centers, namely, areas of active lymphopoesis. Some of these areas are circumscribed simulating normal germinal centers, while others are largely ill-defined sheets or islands of lymphopoetic tissue. Among those islands are relatively sparse areas of lymphoid pulp composed predominantly of small lymphocytes. Mitotic figures are numerous in the germinal centers. The tumors' tissue does not extend into the muscularis nor into the superficial layer of the stroma. There is, however, some inflammatory infiltration in these zones with lymphocytes and plasma cells predominating. The histological diagnosis is lymphosarcoma of the urinary bladder.

DISCUSSION

The extraordinary rarity of lymphosarcoma of the urinary bladder is due to the fact that the normal bladder lacks lymphoid tissue. It requires prolonged irritation through infection before true lymphoid tissue appears in the submucosa. One or two attacks of cystitis are not enough. Even then structurally complete lymphoid tissue appears only in a small percentage of cases. The appearance of a bladder in which lymph-follicles have developed is typical. With the naked eye many small rice-grain-sized, white bodies are seen. They are usually situated at the trigone, but they might cover the whole bladder mucosa. The terms follicular and granular cystitis have been used. Figure 4 shows a tiny, isolated lymph-follicle which was found in a chronically infected bladder. It could not be seen with the naked eye. Figure 5 shows the more complete develop-

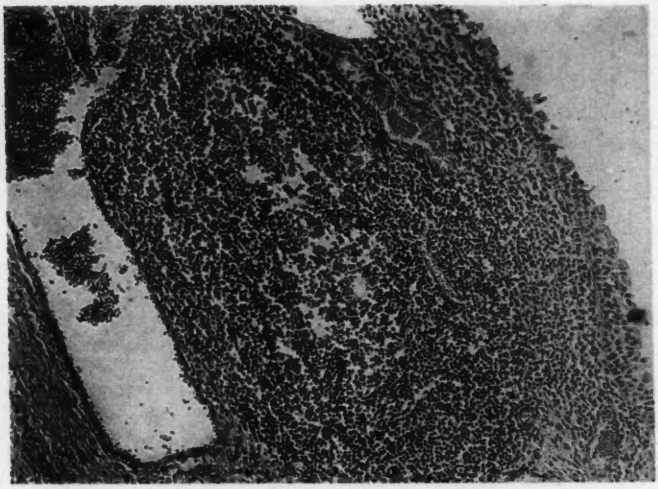

Fig. 5. Large lymph follicle in bladder.

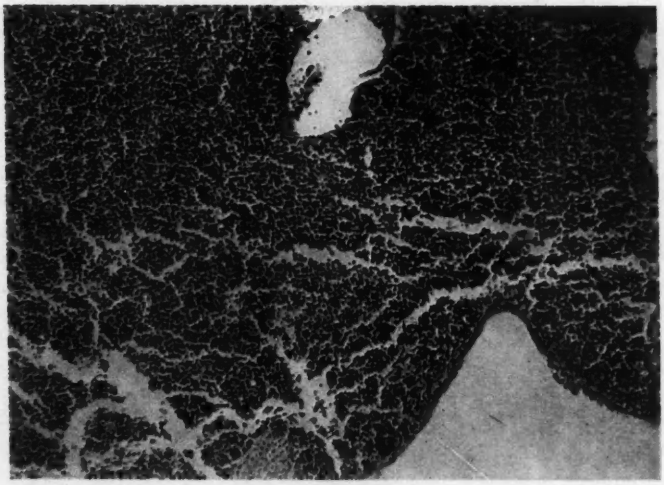

Fig. 6. Lymphosarcoma of prostate.

ment of follicular cystitis. The specimen is from the bladder of a female with a history of long-standing cystitis. The follicles could be seen with the naked eye and looked like tubercles.

It is significant therefore that in all cases of lymphosarcoma of the bladder reported so far cystitis symptoms have been present for various periods. In Eve's case symptoms had been present for several years, in Chaffey's for two years, in Maragna's for many years, in Dupont's and Misrachi's for seven months, in Kreutzmann's for twenty-five years and in ours for ten years. The development of a lymphosarcoma from these secondary lymph-follicles in the bladder is an exaggerated inflammatory and regenerative overgrowth of those particular tissue cells. It is to be expected that these tumefactions vary in their degree of malignancy. The first three cases reported probably were quite malignant. On the other hand Dupont's and Misrachi's, Kreutzmann's and our case hardly could have been malignant types of growth. Recovery took place in all three. The question of accurate diagnosis has to be considered too. It is almost impossible to give a definite critical opinion on the descriptions and illustrations of the previous five cases. Our slides were also examined by the late Dr. Ewing who agreed with the diagnosis of lymphosarcoma. He added that the growth did not appear to be very malignant and that probably no recurrence would take place.

Lymphosarcomas are usually classified as belonging to two types: (1) The large cell lymphosarcoma, commonly called the reticulum cell lymphosarcoma which arises from the germinal center lymphoblasts and (2) the malignant lymphocytoma which consists of a primitive type of lymphocyte. Borst has made three classifications. His first group is the most malignant one; it consists of the pure reticulum cell tumors the cells of which anastomose and are of the most primitive form. The second group is of a lesser malignancy; its tumors contain lymphoblasts of a more mature type. The third group contains the lymphocytomas which he considers the least malignant; they are built up by the fairly mature lymphocytic sarcoma cells. The tumor reported here would belong to Borst's second group.

Figure 6 illustrates the more malignant type of large cell lymphosarcoma. The slide is taken from a prostatic tumor which was reported by Rathbun and de Veer in 1938. Here we have scant

stroma, masses of large lymphoblasts with marked anaplasia and no lymphoid pulp.

SUMMARY

The sixth case of primary lymphosarcoma of the bladder is reported.

It was a mildly malignant growth which was treated surgically and with roentgen rays. It did not recur within six months.

The pathology and etiology of vesical lymphosarcoma are discussed.

DISCUSSION

DR. WILLIAM C. QUINBY: Apropos of these most interesting reports of retroperitoneal tumors, other than those of the kidney, by Dr. Herman and Dr. Hoch, I wish to relate very briefly and show slides of an interesting patient, a woman of thirty-nine, who had increasing hypertension for three or four years. There had occurred marked eyeground changes, headaches, and all the various phenomena that accompany increasing hypertension. She had been carefully observed but had never had an intravenous pyelogram made. On studying intravenous pyelograms, however, it became immediately evident that her left kidney was pushed out of position by a mass above it. This mass was removed and found to be a large pheochromocytoma, a tumor of the adrenal medulla. It is common knowledge, of course, that such tumors cause hypertension, but usually this has been of the paroxysmal type. A person going along quite well, as far as his general life is concerned, suddenly has an acceleration of hypertension with flushing, headache, and great distress lasting a few hours and followed by remission. In this patient, however, the hypertension was of the other type and was continuous and progressive. This is the first point the case illustrates.

My other point is shown in a slide of this tumor treated by a new differential stain reproduced in color [Slide]. You see here the tumor; if you look closely, the brown is the blood, and the green is the chromaffin-staining material which is characteristic of such tissue, whether it be in the carotid body or the adrenal medulla or elsewhere. This seems an advance in the histological demonstration of these various unusual types of tissue.

DR. BENJAMIN S. BARRINGER (New York, N. Y.): I should like to speak of one phase of this series of extremely interesting papers, that is Dr. Hoch's suggestion of removal of an adult kidney tumor showing metastasis. I think there are two reasons that on occasion this should be done. In the first place, an adult kidney tumor, hypernephroma or adenocarcinoma, is radio-insensitive for two reasons: (1) The cells are radio-insensitive, and vigorous blood supply hinders any obliterating endarteritis by x-ray therapy. (2) The metastases are very often radiosensitive. I have had one case

in which I believe I probably was able to sterilize the kidney tumor, an adult kidney tumor, with metastasis. By sterilization I mean the tumor was probably replaced by scar tissue. The patient died at the end of about two years of some obscure x-ray effect on the intestinal tract.

The second patient is living now after about two and one-half years. She has a large kidney tumor with a left supraclavicular metastasis; nothing in her lungs. I took the kidney tumor out, and beyond my reach, where I could just touch, was an area of tumor about 10 by 10 centimeters. I couldn't remove it, I couldn't reach it. I could just simply be aware of it. The patient was treated by deep x-ray therapy over this area. She had a right supraclavicular metastasis later which was treated with deep x-ray therapy. She has remained perfectly well for about two and one-half years. I believe that her life has been prolonged by the removal of the original growth and the x-ray therapy of the secondaries. I think she will eventually die of tumor.

Dr. George F. Cahill (New York, N. Y.): I wish to call attention to two points in relation to Dr. Herman's and Dr. Hoch's papers. The first is that in the type of tumor in Dr. Herman's report he shows another one of the large adrenal cortical tumors with hormonal symptoms. These occur in both sexes and occur more often in older people than does the usual hormonal tumor. Of our six cases, all were in the old-age group and all were malignant. The second point is that the usual cortical hormonal tumor is frequently benign.

We have attempted to explain why some of these cortical tumors are hormonal and others are not by a study of the normal physiological life cycle of the adrenal cortical cell. That is early spindle shaped; later it becomes enlarged and full of lipoids and discharges the lipoid hormones and then degenerates and disappears. The type of cell varies with the non-hormonal symptoms or the type of hormonal symptoms.

In the medullary tumors, likewise, the tumor is either hormonal or non-hormonal, according to the type of cell. The hormonal tumors are usually benign. We have had only one malignant pheochromocytoma. The non-hormonal tumors are usually malignant; and the more malignant ones occur in infancy, while the more benign occur in adult life.

PRESIDENT RATHBUN: I will ask Dr. Herman to close.

DR. LEON HERMAN: I should like to thank Dr. Cahill for his discussion. The patient with neuroblastoma is alive and apparently well one year after her operation.

(No further remarks by Dr. Hoch and Dr. Wehrbein.)

THE ARMY GENERAL HOSPITAL

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There are two types of general hospitals: those that are designated by number and those that are named.

The numbered hospitals are intended for foreign service and are located well behind the combat area. Several of these hospitals are now in operation in England, Africa, and the South Pacific. They were called base hospitals in the last war. The modern war of movement has interfered with the operation of large hospitals and has resulted in the development of several types of smaller mobile units.

The named general hospitals are located in the continental United States and its possessions. They are larged fixed installations varying in size from 1,000 to 3,000 beds and are intended for the care of casualties returning from abroad. We are planning to evacuate our wounded back to this country as rapidly as facilities will permit in order to reduce our supply problem.

The general hospital performs several functions that are not ordinarily assigned to other hospitals; for example, the separation of officers from the service for physical and mental disabilities, as well as their reclassification for limited duty.

The organization of the professional staff is similar to that found in many civilian general hospitals. There are two main services—medicine and surgery. The services are usually headed by a lieutenant colonel and functioning in each service are the sections, representing the various specialties. Chiefs of sections are usually majors. In some of the larger hospitals, eye, ear, nose and throat, x-ray, and neuropsychiatry are separate services.

The general hospital offers the urologist a good opportunity to do urologic surgery. In many of the smaller type hospitals the urologist devotes most of his time to the treatment of venereal diseases.

Almost every medical officer has one or more military duties assigned to him in addition to his professional duties. During the past year I have been a member of a General Court Martial, Nurses

Retiring Board and have made numerous surveys of missing property and attended the Chemical Warfare School.

I am indebted to General Sheep, the commanding officer, and to the Signal Corps for the slides I am showing today. They are views of Lawson General Hospital, Atlanta, Georgia, where I was assigned to the urologic section for one year. I have recently been transferred to the Fletcher General Hospital at Cambridge, Ohio.

Most of the general hospitals are of the cantonment type of construction—multiple small buildings, joined by covered corridors. Lawson has seventy-eight buildings and a capacity of 2,000 beds. My first impression on seeing the hospital was that the small buildings would be hot and poorly ventilated in summer. However, these buildings are provided with suction fans in the roof and they are very comfortable.

In several instances, the Army has taken over large hotels and converted them into general hospitals, such as those found at White Sulphur Springs, West Virginia; Augusta, Georgia; and Palm Springs, California.

The operating rooms for major surgery are equipped with modern instruments and fixtures. The flooring is well grounded and is made of a composition containing copper filings which is poured over two fan-shaped arrangements of copper wire which in turn are grounded. The switches are all shock proof. The operating rooms are air conditioned. There is a well-trained staff of professional anesthetists.

The cystoscopic tables are of modern design with shock-proof tube. An x-ray technician is on call at all times for taking pyelograms. A good selection of cystoscopic instruments is available.

The urologic section occupies seven wards. Two are reserved for surgical cases (about sixty beds) and five are used for drug-resistant gonorrheal cases. The surgical wards are provided with female nurses who are assisted by trained enlisted men from the medical detachment. The sanitation and general care are excellent. Private rooms are provided in some of the wards to accommodate patients who are acutely ill.

The fever therapy department is operated by the Department of Physiotherapy. But for various reasons it has been assigned to the urologic section. Fever therapy is used in the treatment

of drug-resistant gonorrhea cases. We have had a good opportunity to study the results of the present methods of treatment of gonorrhea. Some of our observations briefly are as follows:

Sulfathiazole is probably just as good and much cheaper than any other drug available at the present time.

If a new case does not respond to sulfathiozole within seventy-two hours, there is little or nothing to be gained by continuing the drug. A change is made to sulfadiazine which will cure an occasional case that does not respond to sulfathiazole.

Small doses, i.e. 6 gm. daily, are just as effectual as larger ones, and high blood levels are not required for cure.

The percentage of cures in new cases was just under 80 per cent.

In those cases not responding to chemotherapy, fever therapy as prescribed by Gen. Hugh Morgan was used. Briefly it consists of:

(a) Withdrawing all medication for one week. During this period a careful medical check-up is carried out.
(b) The administration of 7 gm. of sulfathiazole during the eighteen hours preceding fever treatment.
(c) Raising the fever to 105 F. for five hours.

The results were surprisingly good, and of those who were able to withstand the treatment four-fifths were cured in the first treatment. Those not responding favorably had repeated treatments at weekly intervals. This technique is not without hazard. Many patients had to be removed from the box before completion of the treatment, and one fatality occurred in the first 250 cases treated.

The Technicians' School is located near the hospital and is part of the Command. In this school, enlisted men are trained as technicians and in various other types of hospital functions. They are all high-school graduates, and reports from the front indicate these men are doing splendid work, particularly in the foreward area where nurses are not usually sent. This school has a capacity of 1,200 students. Some of the enlisted personnel of the General Hospitals are being replaced by men on limited service. Members of the WAC are also to be used for this purpose but to date none has arrived.

To date we have had very few casualties. Most of our surgical cases came from the large troop concentrations in the South. The hospital was about 60 per cent evacuated in September in anticipa-

tion of a large number of casualties from the African invasion, but fortunately no large number materialized.

The few urologic casualties I have seen were injuries to the urethra. They were produced by crushing injuries to the pelvis, and we had two cases of shrapnel that had penetrated the perineum and severed the urethra.

This seems to be an orthopedic war so far. The orthopedists had more surgical beds than all the other surgical specialties combined. The severe obstacle courses, mechanized equipment, and airplanes are pretty severe on bones and joints.

RENAL LESIONS WITHIN THE DRAFT AGE

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The condition of the kidneys determines to a great degree the status of the male individual in his calling to participate in the duties of the Federal Service. In would be difficult to elicit all the facts of the draft boards concerning the renal health of men between the ages of eighteen and thirty-eight years without divulging secrets of the boards. Since most men with renal lesions would be culled out and referred to the urologist for determination of renal status, the author has taken from his file all cases of renal lesions in the male within these age limits. The facts pertaining to the WAVES and WAC have purposely been omitted. One can hardly expect to determine the renal health of all men in the draft age from this study alone, because some patients suffering from renal disease would be attended by medical specialists and others by general surgeons. However, it is hoped that this study may stimulate a more exact determination of the renal health of young adults in this country. In order to simplify the numerous related facts, this study is limited to lesions of the kidney and does not include lesions of the lower urinary tract and the genital organs.

This study becomes more important when we realize that in general the Federal Service will not accept for unlimited service a draftee who has but one kidney by congenital or acquired means, who has a skin incision over either kidney, or who is known to have any kind of a "surgical kidney" or who has a metabolic or infectious renal lesion. These categories include renal calculus, unilateral and bilateral; hydronephrosis; acute and chronic pyelitis; pyelonephritis; acute and chronic nephritis; nephrosis; nephroptosis; renal fistula; all traumas of the kidney; ectopic kidneys, with or without symptoms; renal tumors; hypoplastic kidneys; and certain renal anomalies, such as horseshoe kidney, aberrant arterial renal supply with symptoms, duplication of the pelvis and ureters, aberrant ureters, and polycystic kidneys. It is quite evident that, up to the present time, men with minor renal lesions or men who have recovered from such lesions whose general health is good and

who have a reasonable chance of continued good health may be accepted for limited service.

This study includes 330 cases of men between the ages of eighteen and thirty-eight years with renal lesions.

TABLE I

Calculi (renal and ureteral)	154
Pyelitis and pyelonephritis	43
Hydronephrosis	29
Traumatic lesions	29
Tuberculosis	21
Nephritis	16
Hematuria of undetermined etiology	12
Anomalies	8
Ptosis	6
Phosphaturia	4
Nephrosis	3
Perirenal and perinephritic abscess (1 each)	2
Tumor	1
Polycystic kidney	1
Albuminuria	1
	330

Calculi.—It will be seen that renal and ureteral calculi comprise almost 50 per cent of the lesions. Ureteral calculi were included, because it was evident from the history and from the cytoscopic and x-ray findings in these cases that the ureteral calculi began their existence in the kidney. There were 154 individuals with renal and ureteral calculi in this age group. Fourteen patients (9 per cent) gave histories indicating a familial factor. Eight patients gave histories suggesting that they had had renal calculi in the pre-draft age. Fifty-nine had had symptoms for six months or less; the remainder, all the way up to twenty years. The older the patients, the more frequent was the occurrence of calculi. There were six patients in the latter part of the second decade; sixty-five patients in the third decade; and eighty-three from the thirtieth to the thirty-eighth year. This finding practically parallels Kretschmer's series in the frequency of ureteral calculi. The chemical composition of the calculi was not determined in the early cases and is not included in this study, although it is a recognized fact of value. Infections existed on admission or appeared sometime during the passage or removal of the calculi in thirty-three patients (34.5 per cent). Bilateral ureteral calculi were found on admission of the patients in only five instances. Recurrent calculi in the same kidney

occurred in thirteen cases and in the opposite kidney in six patients. One patient was free of calculus formation for a period of sixteen years before recurrence.

Forty-four patients with renal or ureteral calculi (29 per cent)

TABLE II—ASSOCIATED PATHOLOGICAL CHANGES WITHIN GENITO-URINARY TRACT

Hydronephrosis:	
Unilateral	13
Bilateral	2
Pyrogenic renal infection:	
Unilateral	4
Bilateral	2
Pyelonephritis, bilateral	2
Ureteropelvic obstruction:	
Unilateral	2
Bilateral	1
Nephroptosis	1
Aberrent vessels, bilateral	1
Bifid pelvis, unilateral	1
Dilatation renal pelvis	1
Nonfunctioning opposite kidney	1
Congenital absence kidney	1
Albuminuria	1
Ureteritis, unilateral	3
Contracture of ureter	1
Hydro-ureter, unilateral	1
Stricture of ureter, unilateral	1
Bladder calculus	1
Diverticulum of bladder	1
Chronic cystitis	1
Urethral stricture	1
Urethritis	1
Prostatitis	1
Genital tuberculosis	1
Hypospadias	1
Total	47

had associated pathological changes within or outside of the genito-urinary tracts.

Treatment consisted of a nephrectomy, immediate or eventual, in eleven patients; surgical removal of the calculus in thirty-seven; and cystoscopic removal in seventy-eight patients (50 per cent). The stone passed spontaneously in eleven patients. Surgery was advised but refused in three cases; and fourteen patients were never seen after the initial visit. The greater percentage of the patients

were placed on a rigid regime of 4000-5000 c.c. of water per day. The use of distilled water and Vitamin A therapy were encouraged. This may be empirical treatment, but it is not always possible to

TABLE III—ASSOCIATED PATHOLOGICAL CHANGES OUTSIDE GENITO-URINARY TRACT

Pulmonary tuberculosis	2
Sinus infection	2
Lobular pneumonia	1
Duodenal ulcer	1
Ankylosis, traumatic, left hip joint	1
Mesenteric lymphadenitis with calcification	1
Arthritis	1
Chronic tonsillitis	1
Diabetes mellitus	1
Total	11

cause patients to follow an absolute chemical diet to prevent the chemical formation of their renal calculi, except cystine stones.

Pyogenic Infection.—The group of cases of pyogenic renal infection comprises thirty-eight cases of pyelitis and five of pyelonephritis. Eleven of the pyelitis cases were infected with Staphylococcus aureus; twenty-two, with B. coli; one, with B. alkaligenes; and one, with B. mucosus capsulatus. Three histories did not specify the type of infecting organism. In fourteen cases the infection was bilateral. In general, the source of the infection was obscure. One patient had a sinus infection; and another, an infected injury. All were treated conservatively with drugs by mouth and occasional kidney lavage for the prolonged infections. Twenty-four patients were entirely cured of their infection; eight were improved; two, unimproved; and four were seen only once or twice. Very few of these cases were treated with the sulfa drugs.

Pyelonephritis.—There were conspicuously few pyelonephritic patients, five in number. Two had bilateral infections with moderate elevation of systolic blood pressure. Two were treated with nephrectomy; one recovered; the other died in three years. The other three improved, but the infections never completely subsided.

Hydronephrosis.—Hydronephrosis in early adulthood in the male is a comparatively common lesion. It occurred in twenty-nine patients in this series (8.8 per cent). A familial factor was not elicited in any case in this group; although it must be admitted that

there was a congenital factor in eight instances, because the pain in the kidney developed in childhood, and there was complete destruction of the kidney. Eight patients had bilateral lesions. Sixteen patients had symptoms of less than one year's duration, while one had had periodic symptoms for twenty-six years. Only two had slight elevation of blood pressure. Eight were treated with a nephrectomy; and twelve, with various plastic procedures on the ureteropelvic junction and nephropexy. Four were treated by dilatation of the ureter. There was no record of the type of treatment given five patients. Twenty were cured; four were improved; and the result in five cases was not ascertained.

Trauma of the kidney occurred as frequently as hydronephrosis. Twenty-three of the twenty-nine patients were in their early twenties. Most of them were injured in automobile accidents or while playing football. Twenty-four recovered with expectant treatment. Five had a nephrectomy—one, one hour after injury; one, two hours; one, two weeks; one, one month; and one, twenty-four years. Five patients developed infections of the injured kidney, one a B. coli and four Staphylococcus aureus. There were no deaths. Most of the patients were cystoscoped upon healing of the kidney. The pelvis apparently healed completely. However, the function of two of the healed kidneys was diminished, as indicated by the functional phenolsulphonephthalein test. All infections were controlled.

Tuberculosis.—Tuberculosis of the kidney occurred twenty-one times. In three instances, one parent had died of tuberculosis. Bilateral renal disease was present in five patients. Fourteen, or two-thirds of the patients, were under twenty-five years of age. Ten patients had active tubercular lesions either in the lungs, epididymes, internal genitalia, joints or intestines. Only three had symptoms dating back to the eighteenth year or earlier. Thirteen patients were treated with a nephrectomy and partial ureterectomy, ten on the right side and three on the left. The results show that twelve patients are apparently well. Three are living with tuberculosis; five have moved away, and their present condition is not known; and there has been one death.

Nephritis.—Patients with nephritic lesions have not been frequent visitors to the urological clinic until recently. The awakening of the idea of a thorough investigation in all cases of renal

disease has increased the number of these patients. The small number of sixteen patients in this series were for the most part recent arrivals. Three of them showed a familial history of renal disease. Thirteen had elevations of blood pressure. In three cases blood pressure readings were not recorded, although the symptoms and urinary findings of albumin, blood and casts were characteristic of hypertensive lesions. None had symptoms of more than four years' duration. One patient had a nephrectomy for a severe unilateral nephritis with improvement for two years but died in five years of nephritis of the remaining kidney. The others failed to show more than temporary improvement. The cause of their nephritis was not clear, although there were suggestive factors in histories of prostatitis, tonsillitis, pharyngitis, renal infection and diabetes mellitus.

Hematuria.—Hematuria of unexplained origin occurred in twelve patients. Thorough investigative measures were employed and repeated without determining the etiological factor. The father of one patient had had pulmonary tuberculosis, and the niece of another had passed stones. None of the patients passed stones or had an infection of any kind in the urinary tract. Their hematuria ranged from three days to two years. For associated pathological changes, one patient had a peptic ulcer, another spina bifida and a third a splenomegaly, while two had mild pulmonary tuberculosis. All hematurias cleared within one to six months by instillations of 1 or 2 per cent silver nitrate solution into the kidney pelvis.

Anomalies.—Anomalies of the kidneys were infrequent—more infrequent than in the average group of patients examined. One patient had crossed ectopia, two had duplication of the kidney pelvis and ureter, and one had an ectopic kidney lying within the bony pelvis. Two had congenital absence of a kidney; two, hypoplastic kidneys; and one, a horseshoe kidney. For symptoms, seven had pain in one kidney; and one patient had albuminuria.

Nephroptosis.—Ptosis of the kidney in the male is rare. One patient, an Army captain in World War I, had had an Hibbs operation without relief of "back pain" but was relieved by a nephropexy. Five of the six patients were past thirty years of age. The symptoms of pain in the kidney ranged from three weeks to ten years in duration. Only one patient had a surgical nephropexy.

The others were not treated, and the disposition of their problem was not made, because they were seen only once.

Phosphaturia.—A diagnosis of phosphaturia was made in four cases. The ages of the patients were twenty-one, twenty-seven, thirty-six and thirty-eight years. Their symptoms and signs of urinary irritation and frequency with small bladder capacity extended from five days to twelve years with visits to many physicians without relief. None had uninary infections or calculi demonstrable by cystoscopic and x-ray examinations. Three were controlled with ingestion of dilute hydrochloric acid while the fourth failed to show much improvement after two months of therapy.

Nephrosis.—Nephrosis as such occurred in three patients. In one patient there was a familial history of cardiorenal disease. The other two had histories of prolonged symptoms of seven years or more. They showed albuminuria, low specific gravity of the urine, diminished renal functional test and elevated blood pressure. They were all treated in a conservative manner without any appreciable improvement.

Perirenal abscess and perinephritic abscess were present on one occasion each. Both patients recovered with incision and drainage. *Albuminuria* was the sole finding in one patient of eighteen years. This persisted and may have been a warning that a nephritic lesion was in the making. *Kidney tumor* occurred only once. This is conformative with the general opinion that renal tumors are least common in these decades. The single occurrence of renal tumor was in a twenty-seven-year-old patient. The tumor was a very large one, was reduced in size by x-ray therapy, and was surgically removed. The pathological diagnosis was hypernephroma. The man is well after a nine-year period.

There was only one patient with *polycystic kidney disease.* He was thirty-one years of age and had been refused life insurance because of albumin and elevated blood pressure. His renal function was good. His blood pressure was 180 mm. Hg. systolic and 124 diastolic. The left kidney was about twice normal size and showed the typical pyelographic pattern of polycystic disease. The right pyelogram and renal outline were entirely normal.

The peak of adult renal health undoubtedly occurs before the fortieth year. An attempt has been made to determine the most

common renal lesions seen in the urological specialty during the draft age. These statistics are from civilian life and not from the governmental services. Thirty-one, or almost 10 per cent of the patients, either had a familial factor of renal disease or symptoms of renal disease before the age of eighteen years. There is good evidence that renal calculi comprise about 50 per cent of the renal lesions which occur during the draft age and that recurrence of renal calculi in the same kidney or the opposite kidney occurs in 12 per cent. Renal infections are common, with a high percentage of staphylococcal infections. Tuberculosis of the kidney was found in 6 per cent of all the cases in this series. Emmett and Kibler have well demonstrated in their study of a large group of patients with renal tuberculosis that this disease is most frequent in the fourth decade and that it is twice as common and twice as serious in the male as compared with the female. Nephritic lesions and hypertensive syndromes were relatively uncommon. A relatively large number of unexplained hematurias was encountered which cleared without further evidence of disease. As would be anticipated, renal injury occurred most frequently in the early twenties, at the age of greatest prowess.

One might anticipate that, since 90 per cent of these cases did not show any stigma of renal disease at eighteen years of age, the statistics of renal disease in the Federal Services would nearly parallel the above figures. However, draftees who have careful physical examinations together with x-rays of chest and abdomen and who lead an exemplary life in the service with the best of food might be permitted to experience unusual renal health in this age group. What renal lesions will develop from shock, nervous strain, endocrine disturbances and complications as sequelæ to bodily injury in war one can not foretell. However, it is quite evident that the government has set the draft age of eighteen to thirty-eight years at a period when renal disease is at its lowest figure and expectancy of renal health at its greatest period. It is hoped that this presentation may be a stimulus to further study of renal disease and promotion of renal health in the young adult.

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MALIGNANCY OF THE EPIDIDYMIS

WITH REPORT OF A CASE OF TERATOMA OF THE EPIDIDYMIS

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Malignant disease of the epididymis does not find a place in the indices or as far as I can find from perusal in eight of ten texts on pathology. The exceptions are Ewing's *Neoplastic Diseases* and Stout's publication. Some space is devoted to this subject in each of the more recently published texts on urology but authors' statements are greatly at variance with each other. All this occurs at a time when there have been accumulated approximately half a hundred cases of malignancy of this organ many of which are well reported, the primary nature of the growths proven, and end results compiled. Primary neoplastic diseases of the epididymis rate a section in texts on pathology and should be considered more fully in accord with now known facts in future revisions of texts on urology and in new publications.

Tumors of the testicle and of the organs derived from the embryonic genital ridge can not be considered entirely independently of each other. The latter group consist of the testicular tunics, the epididymis, and the spermatic cord. Although derived from separate germs layers these organs are not only juxtaposed but also the latter organs, in both the male and female, are commonly found to contain cell rests of germinal cells. Such cell rests are usually benign but have malignant potentialities. Ewing[6] says of these that malignant tumors which originate from cell rests in parts of the genital chain are possible but should be less common than in testes and apparently are so. This statement accords with the clinical fact that malignant tumors of the testicle are common while those of the epididymis, tunics, and cord are very rare. He further states: "Which if any of the malignant epithelial tumors may originate from fully differentiated cells of rete, epididymis, or testes remains for future observations to determine."

The cell structure of malignant tumors of the testicle together with their clinical course stamp them as an unique group. Chevassu

was of the opinion that the large, round cells with clear cytoplasm, so often seen in tumors of the testicle, closely resembled spermatocytes. He called such tumors seminoma. This point of view seems not to be entirely acceptable to most pathologists. Ewing[6] states something of the same concept—"In the testicle, more notably than in any other organ, it is possible to maintain a single embryonic origin for the great majority of tumors." Such tumors are usually teratoid in type with overgrowth of one type of cell. Ewing prefers the term embryonal carcinoma.

Because of numerical preponderance of testicular tumors it has been possible to determine both their pathology and clinical behavior. Up to the present the number of malignant tumors of the epididymis has been so small that their pathology and origin have been less well determined and no attempt has been made until recently to establish end results. The highest figures mentioned for the total number of cases available in the literature is ninety-two (O'Brien[12] quotes Gilbert's personal communication). Lazarus[10] (1938) found forty. Strong[13] (1942) reported a primary rhabdomyosarcoma and O'Brien a case of sarcoma in 1942. Mackay[11] (1943) recorded two more benign tumors. Excellent reviews of the literature have been made by Hinman and Gibson[9] in 1924 and Thompson[14] in 1936. The latter author found 40 per cent of primary tumors of the epididymis to be benign and 60 per cent malignant. Hinman and Gibson found sarcoma to be the most frequently encountered primary malignant tumor of the epididymis and tumors of epithelial origin second in the ratio of twenty to eight. Thompson reversed this frequency, finding twenty-three tumors of epithelial type and twelve sarcomata. Data are not now available for statistical classification beyond indicating that carcinomata and sarcomata predominate. Up to the year 1936 it had been frequently stated by authorities that primary dermoid tumors and teratoma of the epididymis did not occur at which time Thompson reported an undeniable case of primary dermoid of the epididymis. He accepted Barringer's[2] case of primary teratoma with reservations as the one case of teratoma in the literature. Three cases which are frequently mentioned are May's, Barney's and the unusual case of Hinman and Gibson which one of the joint authors (Hinman) did not accept as "established" in his text book. Barney[1] did not even claim any epididymal involvement in his original report. In May's case there was both tes-

ticular and epididymal involvement, the tumor large, and the epididymis could well have been involved by extension.

From study of collected cases, embryological factors, and the recent appearance of a report of dermoid of the epididymis it appears probable that eventually there will appear in the literature reports of proven cases of primary origin in the epididymis of all the malignant tumors commonly found in the testicle. This fact, if established, will strengthen the point of view that cell rests in the organs derived from the genital ridge are the source of tumors in them. This point will be very difficult to prove.

The clinical evidence now available does not lend support to the significance of cell rests unless one assigns strikingly dissimilar characteristics to these cells because of displacement. There appears to be a marked difference in rate of growth, tendency to metastasize, and end results in cytologically similar tumors when they occur in the epididymis rather than in the testicle. It has not been possible to produce cures by any means now available in excess of one-third of the cases treated for tumor of the testicle. Most statistics for series fall far short of that figure. In contrast, Thompson notes survival of 77 per cent of thirty cases, one up to nineteen years, of epididymal malignancy. These results have been obtained in some instances through partial epididymectomy alone, epididymectomy sometimes followed by orchidectomy at a later time, and simple orchidectomy in most instances without radiation therapy either before or after surgery. Furthermore, perusal of the histories indicates that many of the malignant tumors of the epididymis have been present for long periods of time before surgical removal. I note that in thirteen cases where accurate data were recorded an epididymal mass was known to have been present for an average of six and one-tenth years; in one patient for two months, in another six months and twenty-two years in a third. A high percentage of the cases reported indicate that the tumor was small and operation was performed because of symptoms, of which pain was commonest, or for recent increase in size of a mass which had been stationary for many months or years. Lazarus found that trauma, which he found in the histories of ten of forty patients, played a part either in producing symptoms in long standing tumors or appeared to activate growth in others. Some of the malignant tumors were so small, clinical evidence of malignancy being absent, and cure was so easily

obtained that they had none of the recognized malignant behavior of testicular tumors. I find no data as to the frequency of accidental discovery of malignant tumors of the epididymis in autopsy specimens although the statement has been made that they have been so discovered. Examination of scrotal contents at autopsy is usually sketchy.

With full appreciation of the uncertain state of knowledge about malignant diseases of the epididymis, in face of denials of the possibility of teratoma arising in the epididymis, but with the conviction that any type of malignant tumor common to the testicle may be expected to occur as a primary tumor of the epididymis I present a case which I consider to be a primary teratoma of the epididymis.

CASE REPORT

The patient was a thirty-seven-year-old dental mechanic, married, the father of a child and claiming normal sexual activity. He had been ill but once that he could remember and that was three years ago when he had whooping cough at the same time as did his child. There were no complications or sequellæ. He had had headaches from diet occasionally but, as a rule, he has been extremely well all his life. The right testicle was retained well into adult life and came down into the scrotum at about the age of twenty-two years.

Six months ago he became vaguely aware of dull pain in the right groin which was not at any time severe or located in the scrotum. He was sensitive about this symptom as far as his wife was concernd, with the result that he gave it no attention for several weeks. He then noted for the first time that there was a small nodule in the scrotum which was not tender but was definitely something new. On admission he believed that the nodule had gradually, but not rapidly increased in size. It had never been tender although the groin pain soon became permanent. He sought medical advice six months after onset of pain because of increase in size of the nodule rather than because of the mild pain.

Examination showed negative general physical findings. The left testicle was of average size and appeared to be normal. The right testicle was approximately half the size of the left, soft, but normal in shape. Attached to the right testicle was a smooth, firm, nontender mass about the size of a pullet's egg. The mass was attached to the testicle, above it in position, and somewhat larger. No structure simulating the epididymis could be recognized. The mass was not transilluminated.

The urine, prostate, and secretions of the prostate were normal. Red blood cells, 4,680,000; white blood cells, 7,600; hemoglobin, 96 per cent; nonprotein nitrogen, 40 mg. per cent; tuberculin test in di-

lutions of 1:100,000 and 1:10,000 negative; Hinton and Aschheim-Zondek tests negative.

The tumor was tapped and 3 c.c. of thick yellowish material removed. Aërobic and anaërobic incubation failed to reveal bacteria. Microscopic examination of the centrifuged fluid revealed no cells. The pathologist reported that this fluid consisted of 4 c.c. of a purulent, greenish-gray fluid. This was spun down and a cell block mount made for microscopic examination. Microscopic examination revealed a small amount of amorphous material like acellular debris containing a small amount of acute inflammatory cells. Diagnosis: No carcinoma cells found.

The patient was admitted to hospital and scheduled for operation with a preliminary diagnosis of tumor of the epididymis.

Operative Note.—At the lower pole of a small but apparently normal testicle was found a round tumor measuring about 2 cm. in diameter which was firm with semi-fluctuant areas. The field of operation was guarded with sponges and the tumor incised in a soft area. Some material escaped which was thick but did not appear to be purulent. The walls of the incised soft spot were thick and situated either in dilated tubules of the epididymis or in cyst cavities were papillary-like tumor masses. The testicle seemed to be totally uninvolved in the tumor formation. This appears to be a tumor with cystic chambers the nature of which I do not know. An orchectomy was done. The scrotal wound was closed without drainage.

Subsequent hospital course was uneventful. The patient was discharged with a healed wound on the eighth day after operation.

The patient has been followed since operation and seen within a month of this writing. In the twenty months since operation he has had no evidence of his disease except the scar of the operation.

Pathological Examination: (Dr. M. T. Schlesinger) The specimen (Fig. 1) consisted of a testicle including epididymis, all inclosed in a tunica vaginalis. The testicle measured 6.0 by 3.5 by 2.5 cm. and was practically inclosed by the tunica vaginalis. This sheet of tissue was a pinkish red color, externally, and somewhat irregular. There were numerous fibrous shreds attached to it. The undersurface of the tunica, that portion which comes in contact with the testicle, was pinkish gray, smooth and glistening. This represented the tunica albuginea. The lower 4 cm. of the testicle felt soft and spongy while the other portion felt irregular and nodular. On the posterior lateral surface of the testicle was a small band of tissue which measured 6.0 cm. in length and 0.3 by 0.2 cm. in width and thickness. This represented the head, body, and tail of the epididymis. There was a large amount of fat associated with the epididymis. This was the usual glistening yellowish color. When the testicle was opened, it was seen that the tunica albuginea sent numerous sheets into the parenchyma of the testicle. The testicular parenchyma was tannish brown color and finely lobulated. When

the seminiferous tubules were probed, they were moderately elastic. The head of the epididymis was definitely enlarged and very firm. It appeared as pearly grayish white color. The central portion was a pinkish tan color, very soft and bulging above the cut surface. Frozen section through this area revealed what appeared to be adenocarcinoma of the head of the epididymis. There was no definite gross invasion into the testicular parenchyma.

Fig. 1. Photograph of the right testicle showing teratoma of the epididymis which appears to be primary in that organ and not to involve the testicle.

Microscopic Study.—Five slides revealed a variegated picture. One section showed some loose collagenous connective tissue which was covered by some transitional epithelium the more superficial layers of which were pear-shaped, suggesting bladder mucosa. Another area consisted of numerous epithelial cells arranged in a dense pattern with no clearly defined basement membrane. Another area showed tissue resembling skin in which the stratum lucidum was somewhat thickened, consisting of parallel bands of eosinophilic-staining material. Below this was a layer of stratified squamous epithelium but no rete pegs were present, simply dense bands of collagenous connective tissue below the stratified squamous layer. There was also a stratum granulosum and a stratum germinativum within the skin. There was a rather well circumscribed mass of cartilaginous tissue. This was made up of the usual hematoxylin-staining matrix containing numerous lacunae, containing one cartilaginous corpuscle. There were several glandular components, each of which was lined by tall columnar epithelial cells varying between one and three layers in thickness. There was one long segment enlarged almost to cystic proportions which was lined by tall

columnar epithelial cells. There were numerous ducts lined by tall columnar cuboidal cells. There was one very large cyst lined by tall columnar epithelium in which the cytoplasm took a neutrophilic stain and a very large nucleus lay in the center and basal portion of the cell. This cyst was completely devoid of content.

Another section showed a second area resembling skin and also numerous smooth muscle bands dispersed among some dense collagenous connective tissue. There was one area having a dense spindle-shaped stroma suggestive of ovarian tissue but no other sex cells were detected. There was one area made up of myxomatous tissue suggestive of Wharton's jelly.

Another section showed several large cysts some of which are lined by one, two, or three layers of tall columnar cells. No epididymis tubules are found among these tumor elements.

The testicle was made up of seminiferous tubules which consist of acini which are decreased in size and have slightly thickened basement membranes throughout. There were numerous cells placed along the peripheral edge of these tubules. Most of these cells were very large. Some had a clear, vesicular nucleus and others had a dark-staining chromatic nucleus. There was marked distortion of the seminiferous cell pattern. No sperm was found in any of the tubules. Between the tubules was a loosely arranged stroma of aerolar tissue containing a few capillaries, and a scattering of lymphocytes throughout. Interstitial cells were rare. Scattered throughout were a few completely degenerated tubules surrounded by and infiltrated with lymphocytes. One section showed a definite aggregate of lymphocytes with a germinal center.

In the two sections showing testicle, adjacent to the testicle was a neoplastic tissue which in one spot was definitely in the tunica albacantes. The nearby testicular tissue showed marked degeneration with heavy infiltration with inflammatory cells but no definite recognizable neoplastic elements.

Diagnosis.—Teratoma of epididymis.

DISCUSSION

Primary teratoma of the epididymis, similar to dermoid until the report of Thompson, has not been proven to occur in the epididymis. Thompson accepted Barringer's case with reservations and Lazarus accepted three cases but does not designate which ones he considers proven to be of epididymal origin. The three cases which are frequently quoted as possible primary teratoma do not bear inspection and seem to have gotten into the literature and been easily quoted. These are May's case, Barney's case, and the unusual case reported

by Hinman and Gibson, which have already been discussed. Hinman[8] does not accept any of these as established beyond doubt. Barringer in reporting his case stated that the Cornell clinic had another case of primary teratoma of the epididymis similar to the one he published. Barringer and Dean[3] stated that they had seen two cases in which teratoma grew atypically and involved the epididymis alone, but gave no detailed account of them. Von Lichtenberg's[7] clinic is said to have had two cases in which the teratoma appeared to be primary in the epididymis but the testicle was also involved.

Barney and also Hinman[8] quote Ewing to the effect that teratoma of the epididymis does not occur judging from the reports in the literature. These quotations were both from the first edition of Ewing's pathology (1921).[5]

Ewing[6] indicates that the common site of origin of teratoma testis tends to confuse when the tumor involves both the testicle and the epididymis. He states—"Teratoma testis arises at the junction of the rete and the spermatic tubules, and at this junction Kirkbride has shown that there may be very marked disorder in the structure of the fetal testis favoring displacement of cells." It has not been possible to determine in some cases in which the tumor involved both structures but showed predominance of growth in the epididymis whether that predominance indicated primarity in origin. Bland Sutton[4] reported a tumor made up chiefly of sarcoma cells which appeared to arise *between* the testicle and the epididymis.

In the case here described the small size of the tumor and the preservation of the testicular tunic appears to indicate conclusively that the tumor is primary in the epididymis. I regret that due to loss of the remnants of the tumor in the laboratory serial sections could not be prepared.

CONCLUSIONS

The number and quality of reports of primary malignant tumors of the epididymis justify a place for this subject in the texts on pathology and urology.

There are not now data sufficient to determine whether adult cells of the epididymis can give rise to malignant tumors. It appears that this is possible, at least for certain kinds of tumors.

Tumors which simulate those characteristics of the testicle may and probably do arise from fetal implants of cells from the testicle.

The clinical behavior of primary malignant tumors of the epididymis, especially carcinoma and sarcoma, are not characteristic of cytologically similar tumors when they occur in the testis. When the testicle and the epididymis are both involved clinical progress is more nearly that of tumors of testicular origin.

It is probable that any type of malignant tumor which is common to the testicle may occur in the epididymis but the frequency of occurrence is greatly reduced below that in the testicle.

A case of primary teratoma of the epididymis is recorded.

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DISCUSSION

DR. BENJAMIN S. BARRINGER (New York, N. Y.): I think Dr. Crabtree has given us a new point of view of the origin of these epididymal tumors. That is, they start from rests actually in the epididymis itself. I think that is a very interesting point of view. It is a new one to me. Dr. Ewing, I always understood, believed that all these teratomas started in the rete testis between the epididymis and testicle, and for some unknown reason they mostly grow towards the testicular side. Occasionally they would grow towards the epididymal side, producing an epididymal tumor instead of a testicular tumor. I would be interested in having Dr. Crabtree discuss that.

Just one other word. I once took a paper to Dr. Ewing in which I described malignancy of something or other, and Dr. Ewing with his customary way snorted, pointed his finger at me and said, "There is no such thing as malignancy. There are malignant lesions."

DR. REED M. NESBIT (Ann Arbor, Mich.): I would just like to point out one thing in the discussion of one of the discussors. Dr. Barringer pointed out that Dr. Ewing had said that malignancy could not be used as a noun designating a malignant tumor. We had occasion to look up that word in the 1942 dictionary three or four days ago. In that dictionary it said malignancy is one of the medical terms; malignancy is a malignant tumor, and the word may be used in that way, according to modern usage.

DR. J. DELLINGER BARNEY: I was very much interested in Dr. Crabtree's report of this primary tumor of the epididymis. Since he cited me in this connection, I want just briefly to bring up two or three cases which I reported a great many years ago. Perhaps you know just when it was, Dr. Crabtree.

DR. CRABTREE: About 1925.

DR. BARNEY: 1925. Well, at that time I reported three cases, I think, before this Association, which I had seen in consultation. One man, in 1912 when I saw him, was about thirty years old, lived out West, with every evidence of tuberculosis, except I think they

never found the bacilli in his sputum. He had an epididymitis for which I was asked to see him. He had very definitely, I think everybody would agree, an epididymitis. It was nodular, it was hard and very much enlarged, and you could feel definitely the sulcus between it and the testicle. Not only that, but he had an involvement of the lateral lobe of his prostate on that side, and what I thought was a nodular, indurated seminal vesicle. The picture was clear. I decided it was a tuberculous epididymitis and advised operation. The surgeon said, "No, we will wait."

We sent the man to Saranac where he improved generally, but the testicular condition increased and in a few months' time there was a mass about the size of a lemon. The surgeon then did an orchectomy. That specimen, which I didn't see, was reported by the pathologist, the late Dr. James Homer Wright, of the Massachusetts General Hospital, as being a round cell sarcoma. The surgeon was not satisfied with that, so he sent the specimen on to the late Dr. Ewing. I blush to say I have left Dr. Ewing's letter at home. I can tell you briefly what he said; namely, that there was no evidence of any epididymal tissue anywhere and that he thought it might well be a seminoma. That, briefly, is what he said. The point is, there was no epididymal tissue.

The next case I saw was in 1918. This was a boy of nineteen years, who was thought to have tuberculosis because of various conditions which I shall not enumerate. A surgeon took out his appendix just before this and found a lot of calcified glands in his mesentery. He had an epididymal involvement which I was asked to see, incidentally, with the late Dr. Chute. This, again, was a perfectly typical epididymitis with no involvement of the testicle, so far as Dr. Chute or I could find. Again, I advised operation on the basis of the diagnosis of tuberculosis and, again, the operation was not thought to be wise, until about six months later or something like that, when the mass was found to be the size of a lemon. Then orchectomy was done by another surgeon. Again, I didn't see the specimen, but the report was made by Dr. Wright. It was said to be a combination of embryonal carcinoma and teratoma.

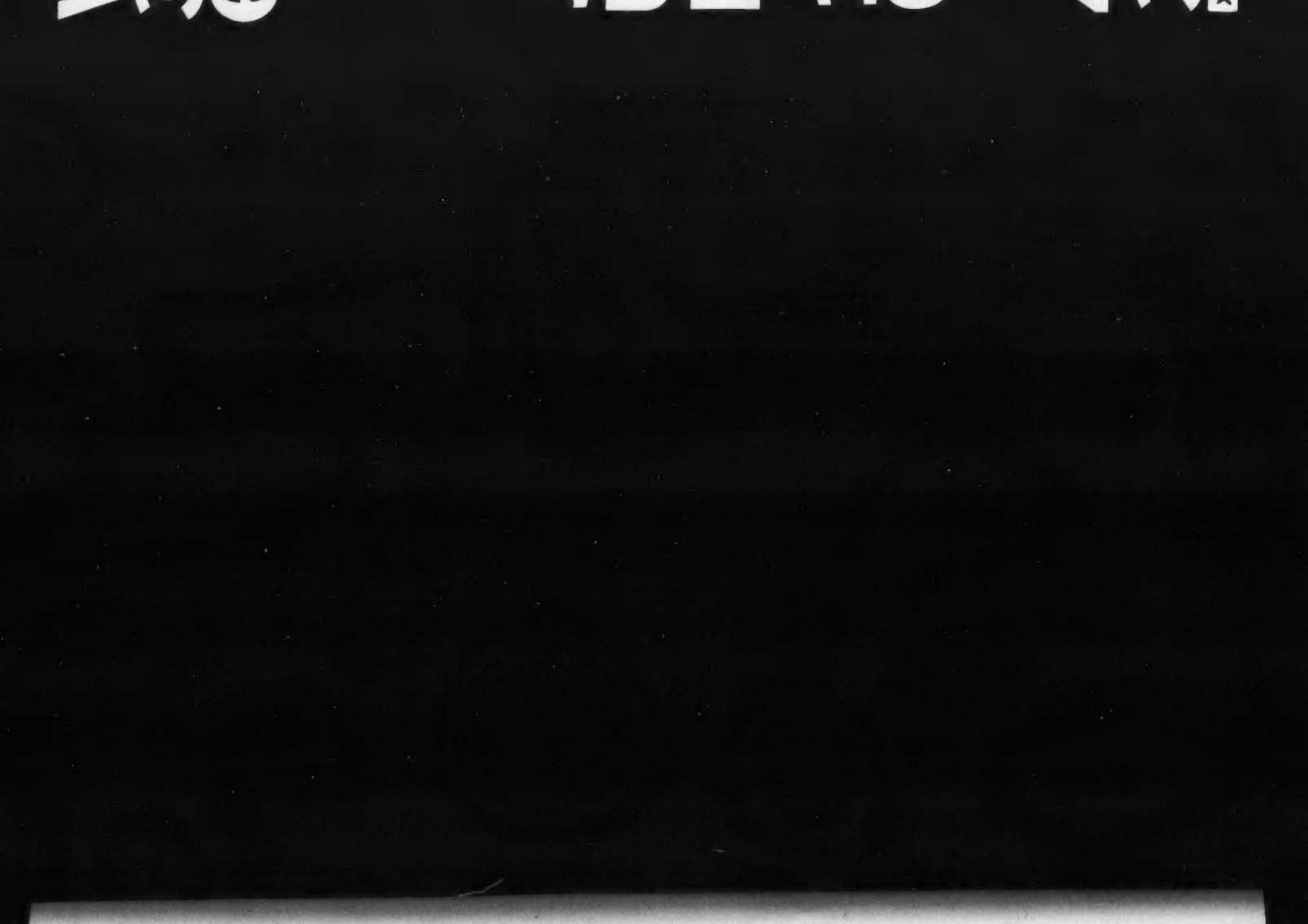
The third case I saw was at the Massachusetts General Hospital. This man with undeniable advanced lung tuberculosis had an epididymitis, and, again, like these other two cases, the testicle showed no evidence of involvement. He not only had tuberculosis, but he

was also a hemophiliac. I refused to operate on him. Finally, he persuaded one of the surgeons at the hospital to operate on him, and an orchectomy was performed. There was no evidence of tuberculosis at all but there was a malignant tumor. I don't know what the diagnosis was. The point in these cases, in my opinion, is that all were involvements of the epididymis, not of the testicle at all, and in two of them, to my knowledge, after the lesion was removed, there was no evidence of epididymal tissue. I don't know that that proves it, but the fact that the epididymis was involved in the first instance with no evidence of epididymal tissue after the situation was made clear, would indicate that there was a possibility that those were primary in the epididymis, and for that reason I think we should all operate in every case where we cannot make a positive diagnosis that the lesion is definitely of a benign sort. In other words, when you are in any doubt—operate, because you may catch these things in the early stage and that, incidentally, will help the patient.

Dr. E. Granville Crabtree (Boston, Mass.): I do not know whether I stand corrected on the use of the term "malignancy" or not. The loyal support of Reed Nesbit has been greatly appreciated. The date 1942 seems to be significant.

Dr. Barringer has attributed to me the concept that teratoma of the epididymis might arise from implants from the testicle. I am not entitled to that honor. I have merely quoted Ewing, who is easily quotable in all matters of malignant diseases of the testicle and epididymis because of his long interest and many contributions in this field. He accepts the work of Kirkbride who in turn demonstrated that in the testes of fetuses in the area of the junction of the rete and the spermatic tubules, where he believes teratomata originate, cell disorder is both common and extreme in degree, which makes displacement of cells very easy indeed.

Dr. Barringer is quoting Ewing's first edition of Neoplastic Diseases, dated 1921, and quoting correctly. He evidently has not read subsequent editions of that volume so carefully.



SECOND DAY, JUNE 11, 1943

SULFONAMIDE ANURIA

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Since the introduction of the sulfonamides for treatment of various conditions, an immense amount has been written in many languages of new information concerning the uses of these drugs. The urologist has been the happy recipient of a drug which is accomplishing the clearing up of various urinary infections, much more simply and more efficaciously than has been possible with his various methods previously. While this drug has become very useful, it also has certain hazards in its use. One of these is the action produced in the individual who takes small doses and develops anuria. This is a condition which may be very serious and an effort is being made to avoid it, if possible, or successfully correct it.

Recently a patient of this type came under my care, which seemed of sufficient interest to present to this Association.

CASE REPORT

L. N., aged forty-two, was admitted to Christie Street Hospital, Toronto, March 15, 1943, with a history of having received sulfathiazole and sulfapyridine for treatment of an acute otitis media. Two days after the onset of his treatment, acute suppression of urine developed and the patient died early on his seventh day. The details of his history are as follows:

On the first day, at 8 a.m., he was given sulfathiazole, gr. 30, and followed with sulfapyridine, gr. 15, every four hours for six doses, which carried him to his second day, 12 noon, when he was transferred to the R.C.A.F. hospital at Trenton, Ontario. A further dosage of sulfapyridine, gr. 15, was given every four hours for four doses.

Suppression developed on the third day and the drug was discontinued after the patient had received a total of 180 gr. or 12 gm. of sulfonamide, made up of thiazole, gr. 30, and pyridine, gr. 150, in forty-eight hours. There was a very slight tenderness in the left kidney area and the left ureter was catheterized, but the cystoscopist could not

pass a catheter up the right side as it was thought to be plugged with crystals. The left pelvis was irrigated but the catheter became blocked. No large quantity of urine was obtained. He was transferred to Christie Street Hospital and was seen by the orderly officer and an intravenous of 5 per cent glucose in normal saline commenced.

The fourth day he was resting quietly in bed with no pain and examination revealed only a very slight tenderness in the left costo-muscular angle. The kidneys were not palpable. Temperature, 100; pulse, 112; respirations, 26; blood pressure 210/95. There was no cyanosis and he did not appear ill. An ear, nose and throat specialist reported that his ear condition had cleared.

It was doubtful in our minds that a ureteral catheter drainage of the pelves of the kidneys would be of use but cystoscopy was carried out on an off chance that it would be of help. No urine was found in the bladder. The right ureter was catheterized but there was a good deal of edema and redness around the left orifice and the catheter would not go up. About an ounce of bloody urine came from the right kidney and it stopped draining. It was thought that the catheter was blocked. It was withdrawn and immediately an effort was made to replace it but this time without success, and the catheter would not go up the left side either.

His nonprotein nitrogen was 66 mg. per 100 c.c. of blood. His chest showed no evidence of any trouble. The intravenous of 5 per cent glucose was discontinued at 3000 c.c. Sodium bicarbonate (500 c.c. of 5 per cent solution) was given intravenously slowly, in an effort to produce an alkalinity and give any crystals blocking the tubules a chance to dissolve. Blood concentration was 2.5 mg. per cent.

The fifth day his general condition was very much the same as the fourth day. Temperature, pulse and respirations were slightly elevated. Blood pressure was 220/100. The nonprotein nitrogen had risen to 80 mg. per 100 c.c. General examination of the chest and abdomen showed no change. There was no tenderness over the kidney areas. His treatment consisted of 50 c.c. of 50 per cent glucose, given intravenously every four hours for four doses. Aminophylline, gr. 15, for one dose was followed in four hours by aminophylline, gr. 7, for two doses. Ephedrine, gr. ¾, was given every four hours. He was given saline purgation.

The clinical picture had changed completely by the sixth day. He was breathing rapidly, was cyanotic with a gurgle in his throat suggesting pneumonia. Examination showed moist râles throughout his chest but no dullness was found. No area of tenderness was found over the kidneys. Slight abdominal distention was present. Temperature, 102; pulse, 140; respirations, 40. Catheterization recovered no urine.

The patient died on the seventh day.

Postmortem examination showed a very acute edema of the lungs but no areas of frank consolidation. The kidneys were not increased

in size, no area of gross change was seen in the kidney parenchyma. The pelvis had a small quantity of bloody fluid in it which showed 62 mg. per cent of sulfonamide. The ureters showed no evidence of collections of crystals. No evidence of change in the heart or other organs was noted.

Microscopic examinations of several areas in the kidneys revealed a fibrinoid material present in Bowman's capsule and the proximal convoluted tubules; some also in the distal tubules. Thrombosis of both large and small blood vessels was present, together with isolated areas of interstitial inflammation as shown by groups of plasma cells. The heart muscle showed no evidence of myocarditis.

DISCUSSION

The problem which faces the urologist immediately he sees a patient with anuria of any cause is to decide whether his patient has the anuria as a result of (1) nonfunctioning of the kidney parenchyma, (2) an obstruction somewhere in the urinary passages, usually due to crystals. This will lead to a distention of the kidney pelvis and a resultant pain and tenderness in that side. If there is much distention the kidney enlargement may be felt. In this type of case the ureteral catheter may be introduced to the area above the obstruction and the kidney increases its output of urine and the patient recovers. It is no great problem to decide whether there is distention of the pelvis. This can be ascertained by tenderness over the distended kidney and the ureteral catheter will relieve the distention. If by any chance the catheter cannot be passed to the distended kidney pelvis, surgery much be resorted to to relieve the distention. If one cannot be sure, one is justified in passing the ureteral catheter. In this patient the presence of the "slight" pain and tenderness made it probable that the pelvis on the left side was distended.

The use of the soda bicarbonate intravenously was an effort to place an alkaline medium in the tubules of the kidney to help dissolve any crystals of the sulfonamide which might be blocking the tubules in the kidney. It is known that solubility of the diazine and thiazole drugs increases rapidly as the pH increases from 7.0 to 8.0. The pyridine drug increases its solubility as the pH goes from 9.0 to 10.0. Of the three, this shows the pyridine to be the least soluble. This is due to the fact that these drugs and their acetyl derivatives are weak acids which ionize and form soluble salts in

the presence of the alkaline. Sulfanilamide is a relatively soluble drug.

There is a feeling among the profession now that a patient who takes one or more of the sulfonamides becomes sensitized and a subsequent dose may cause an anaphylactic or similar reaction. Thus a small dose may produce anuria or profound toxic symptoms. There was no history of this patient having taken one of these drugs previously.

The blood level only reached 2.5 gm. per cent and it could not be due to over concentration in the blood.

Decapsulation of the kidneys was considered on the sixth day but his chest had filled up and it was obviously out of the question. Nephrotomy would not have been of any use as there was no obstruction present.

PATHOGENESIS

Some substance came into contact with the nephon of the kidney which caused it to stop its function. In this case the autopsy showed the presence of a "fibrinoid material" which was unidentified. The thromboses in the blood vessels were not marked and are unexplained, as are also the localized areas of inflammation in the interstitial tissue. Frozen sections did not show the presence of crystals as they have done in some other cases.

There was a small quantity of bloody fluid in the kidney pelves but no evidence of collections of crystals either in the pelves or ureters.

In the Department of Pathology at the Banting Institute in Toronto, some slides of other fatal cases were examined. In one, the organs of the lungs, kidneys and spleen showed areas which were granulomatous and contained giant cells. One group thought these to be the granulomas of glanders, while another group considered the granulomas an evidence of toxicity. In another fatal case of a soldier who had treated himself for gonorrhea and died with anuria, there was a small quantity of fibrinoid material in Bowman's capsule, an eosinophilia in the interstitial tissue and no evidence of thrombosis. Thus, these three cases all have a different microscopic picture of the kidney parenchyma. The cause is thought to be a toxin but what, we cannot say, nor do the fatal cases show a uniform picture.

SUMMARY

A case is presented in which the patient was given sulfathiazole, gr. 30, and sulfapyridine, gr. 150, in forty-eight hours. He developed anuria and died early in the seventh day.

The pathological findings were not marked nor did they seem sufficient to cause anuria and death.

The ureters and tubules were not blocked with crystals.

RECENT CASES ILLUSTRATING DANGERS OF THE SULFA DRUGS

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Recent reports indicate that the already wholesale use of the sulfonamide drugs appears destined to increase. This would seem to be due, not only to a wider application in the therapy of recognized diseases and to the development of new and more effective derivatives, but to the use of these drugs in prophylaxis against infection. On a limited scale the prophylactic use of sulfonamides has been employed by urologists in dealing with problems of indwelling catheters and drainage tubes as well as other specialized situations in which potential infection looms large as a complication. The present trend seems to go beyond such indications. It is known that our soldiers in combat service carry sulfonamide tablets with instructions to take them when wounded. Recent publications tell of widespread use of these drugs in prophylaxis against gonorrhea in soldiers on leave. Pediatric practice in some quarters seems to be leaning toward the routine use of sulfonamides in all upper respiratory tract infections with an eye to cutting down the complications such as acute otitis, pneumonia, and so on.

Here, as with almost every known prophylactic procedure, enthusiasm must be tempered with the knowledge that the procedure itself entails some risk. It is therefore imperative for those of us who are administering these drugs to be fully aware of the dangerous potentialities, and to be alert for the detection and prevention of untoward results.

With this in mind we should like to review a few recent cases illustrating the nature of the dangers involved.

CASE REPORTS

Case 1.—C. W., No. 377982, was a forty-two-year-old colored woman who entered the hospital in diabetic acidosis with signs and symptoms of bronchopneumonia. The blood sugar was 370 mg. per cent, the CO_2 combining power 19.5 vol. per cent, and x-rays showed clouding at the right base. Therapy was promptly instituted to regulate the diabetes and combat the acidosis, and she was started on sulfadiazine for the pneumonia. The diabetes seemed to resist all efforts at control.

On the second day of sulfonamide therapy crystals of acetyl-sulfadiazine appeared in her urine. On the third day her urinary output dropped sharply and the number of crystals increased. Cystoscopy was carried out and the ureters were catheterized with difficulty because of bilateral obstruction of the lower ureters with masses of the crystals. Repeated lavage of the pelves with the catheters left in place succeeded in clearing the urine of crystals, but her course was rapidly downhill and she died on the seventh hospital day. Autopsy showed that the crystalline obstruction had been removed, but there were evidences of acute toxic myocarditis, pneumonia, and pericarditis in addition to focal necroses in the spleen, liver and kidneys, and a widespread parenchymatous degeneration of the renal epithelium, part of which may have been postmortem autolysis.

This brings up the problem of urinary tract obstruction due to precipitation of acetyl-sulfonamide crystals. Much has been written of its prevention and treatment, and the weight of clinical and experimental evidence now seems to favor the view that strong alkalinization of the urine is of value in minimizing precipitation. As a matter of routine we are now using sodium bicarbonate as an adjuvant to all sulfonamide therapy, and we frequently supplement this with a potassium citrate and hyoscyamus "bladder mixture," as well as by encouraging the intake of quantities of citrus fruit juices. This case also well illustrates that when the use of sulfonamides becomes imperative in the face of a diabetic acidosis we must make every effort to overcome the acidosis lest we court the more serious peril of an obstructive uropathy. A third feature of the case is the presence of clinical and pathological evidence of renal damage beyond that which can be ascribed to simple obstruction. This is better illustrated by other cases.

Case 2.—C. J., No. 273663, was a fifty-two-year-old banker, who after a year of observation for mild symptoms of prostatic obstruction, entered the hospital for a transurethral resection. His general condition was good, and on a short period of pre-operative catheter drainage his phthalein output improved from a 35 per cent two-hour total to a 55 per cent total. His nonprotein nitrogen was 30.3. During the pre-operative catheter drainage he was given sulfathiazole in doses of 0.5 gm. four times daily. This was well tolerated. Following resection of 20 gm. of median lobe he continued in good condition but began to run a fever which, on the day after operation, reached 102.6 F. It was therefore decided to resume sulfathiazole, this time in doses of 1.0 gm. every six hours. The fever persisted and the patient rapidly became quite toxic. He became disoriented and developed a rash over the entire body, and then developed anuria. Terminally he became jaun-

diced. The nonprotein nitrogen rose to 96 mg. per cent and the patient died in uremic coma. No autopsy permission could be obtained.

The absence of a pathological study in this case is regrettable. All clinical and laboratory evidence suggests that we were dealing with the now familiar entity of focal necroses scattered throughout the kidneys, spleen, liver and skin as well as other organs, attributable wholly to sulfathiazole toxicity.

Case 3.—C. H., No. 379368, was a sixty-four-year-old colored man who was admitted for investigation of a severe lower back pain. General medical, gastro-intestinal and orthopedic examinations failed to establish any cause for this, but in urological consultation we established the existence of a purulent prostatitis. Aside from pus in the first glass of the three-glass test the urine was negative, and it is to be noted that during his first three days in the hospital while undergoing the examinations he was afebrile. Treatment was instituted combining prostatic massage, long-wave diathermy with a rectal electrode, and sulfathiazole with a 2.0 gm. initial dose and 1.0 gm. every four hours. The back pain was promptly relieved, but within twenty-four hours he began to show an elevation of temperature, reaching 101 F. on the first day and 102 F. on the second. Since no other cause could be found for the fever the order was left to stop the sulfathiazole. This was done and the temperature fell to nearly normal in eighteen hours. By some error in transcribing to a new sheet the sulfathiazole order was reinstated and he again began receiving 1.0 gm. every four hours. Within twelve hours he had a most remarkable attack. He developed acute abdominal pain, not well localized, but making him writhe and groan. He began to vomit and sweat profusely, and his temperature shot to 104 F. Various observers entertained diagnoses of perforated peptic ulcer, acute hemorrhagic pancreatitis, and perforated appendix, but it was wisely decided to follow an expectant course since the reaction seemed typical of nothing. It was discovered that sulfathiazole had been resumed, and this was again discontinued. The fever persisted in the neighborhood of 103 F. for two days, and some observers became convinced that pneumonia was developing and that the severe pain had been pleuritic. Despite the fact that his temperature then began to fall he was started on sulfadiazine, 1.0 gm. every four hours. The temperature then fell to normal and the patient became comfortable and appeared nearly well. On the third day of sulfadiazine administration a second accident occurred. Two tablets of sulfathiazole were carried in to him in lieu of the proper gram of sulfadiazine. The reaction was breath taking. His temperature shot to 103 F. A generalized rigor developed, and the patient stopped urinating completely. No more sulfonamide of any kind was given, and his temperature promptly fell to normal, but his anuria persisted for seven days despite liberal administration of intravenous fluid, caffeine, and the use of renal diathermy. His nonprotein nitrogen, which had previously been 28,

rose to 88 and then to 108. On the eighth day after the onset of anuria his renal output began to increase and slowly came back to normal with an accompanying fall in the nonprotein nitrogen. He was eventually discharged after thirty days in the hospital. The phthalein output was 17 per cent in two hours and the nonprotein nitrogen 40. He has been followed in the outpatient department and is now back at work with a phthalein output of 66 per cent and normal nonprotein nitrogen.

In this case we are face to face with the problem of sensitivity. We have here a patient who may or may not have taken any sulfonamides prior to his admission to the hospital but who promptly evidenced intolerance by reacting to the drug with a fever. A second inadvertent course of sulfathiazole brought on an intensified reaction with fever and a fair facsimile of a surgically acute abdomen. A third exposure to the drug certainly came close to disaster. And yet we see that there was a marked degree of specificity in this sensitivity, since the dramatic reaction to a small dose of sulfathiazole came at a time when the patient was tolerating sulfadiazine without difficulty. It is impossible to escape the conviction that we had artificially achieved a high degree of sensitization of the allergic type in this patient, and that this sensitization was not to sulfonamides in general but to sulfathiazole in particular. We have seen other patients in which this high degree of specificity was not present. A short time ago a patient was referred to us for treatment of a urinary tract infection. He brought a note from his family physician which volunteered the information that sulfathiazole and sulfapyridine had both caused rather bad reactions. Since sulfadiazine was not mentioned we felt that it might be worth while trying in view of its supposed lower toxicity. He was given one tablet (0.5 gm.) experimentally. The result left no doubt in anyone's mind that he was sensitive to sulfonamides as a group. Marked gastrointestinal symptoms developed, with a skin eruption, headache, and general malaise.

Reactions of this type are characterized by being prompt and violent. The renal damage in the case presented in detail seems to have been reversible, and neither of these two individuals seem to have suffered irreparable damage to any tissue. The use of a small test dose would seem to be feasible in evaluating sensitivity of this kind; and in the event of bad reactions proper therapy seems to warrant a good prognosis.

One evidence of sensitization would seem to be a gradually

developing intolerance of the drug over a period of time. One such case was encountered in a man who had a temperature of 103 F. following ureterolithotomy. Sulfathiazole was started and the temperature fell promptly to normal but then gradually began to rise. A thorough survey of his condition yielded no clue to the cause of his fever so long as the sulfathiazole was continued. Finally, he had conjunctivitis and photophobia and the drug was discontinued. The fever and all of his toxic symptoms promptly disappeared. Another case in point is that of a man who was admitted with a calculus impacted in his lower ureter and evidence of infection in the other kidney. He was placed on sulfathiazole, and cystoscopy with ureter catheterization was carried out, resulting in a diagnosis of left calculus pyonephrosis and right pyelitis. In catheterizing the ureter the obstructing stone was pushed back into the renal pelvis, relieving his symptoms. He promptly refused operation and left the hospital. Soon after this the stone again began to pass and he returned to submit to left nephrectomy. Postoperatively, because of fever, sulfathiazole was employed again. The fever persisted and he began to have marked general malaise, anorexia, and violent nightmares. With the cessation of the sulfathiazole all the bad symptoms disappeared, the fever subsided, and he made an uneventful recovery.

There are other cases in which the mechanism of toxicity appears to be different. One patient took a short unsupervised course of sulfathiazole because an insurance examiner told him that he had pus in his urine and a medical friend offered the suggestion that it was probably due to chronic prostatitis and could be easily corrected. He tolerated the drug without difficulty for five days, taking 25 gm. in all. Two days after ceasing the medication he had fever and nausea. His symptoms progressed through violent gastrointestinal distress with vomiting and diarrhea, followed by a generalized rash, and culminated in complete anuria, uremia, and death some two weeks later. Here the pathological studies showed no evidence of focal necroses, but indicated a primary effect on the renal epithelium and interstitium which could be properly called an acute toxic nephritis. There was no warning which could have been heeded while the drug was being taken, and the reparative powers of the body seemed to be incapable of overcoming the damage which was done.

From the experience gained in dealing with the foregoing cases, and others of similar nature that we have encountered, we believe that certain conclusions can be drawn. We believe that there is irrefutable evidence that patients can be sensitized to sulfonamide derivatives, and that the majority of the bad reactions come in individuals who have been sensitized by previous courses of the drug. That this sensitization can be accomplished even by the topical application of sulfonamides is illustrated by a boy who suffered a hand laceration while at work and developed an ulcerative lesion which was treated with 5 per cent sulfathiazole ointment over a period of several weeks by the plant physician. It eventually became a frank cellulitis and he was admitted to the hospital. Here he was given sulfathiazole by mouth, but after having received only 6.0 gm. in 0.5 gm. doses he had anuria and uremia. Intravenous fluids, pelvic lavage, diathermy, and alkalinization succeeded in tiding him over his critical period and recovery resulted. A letter from his former doctor on this subject is particularly illuminating. He stated: "Sometime in June, 5 per cent sulfathiazole ointment was applied to the skin, and about July 3 there was a marked local reaction." We would therefore stress careful history taking as to previous ingestion or topical use of sulfonamides, with special reference to any hint of intolerance.

From the point of view of pathology we recognize three types of renal damage from sulfonamides: first, the frankly obstructive, due to the deposition of crystals of the acetylated drug; second, the widespread focal necrotic type of reaction in which the kidney is only one of many organs involved, but in which the renal shutdown provides the frequently fatal insult; third, an acute toxic nephritis in which focal necroses and crystals are absent, but in which anuria and uremia are the clinically striking features.

In respect to therapy, we urge the early institution of intravenous fluid therapy, with appropriate use of 1/6 molar sodium lactate when acidosis is a factor, and with saline administered in accordance with the blood chloride values. The balance of the required fluids should be 5 per cent glucose. Cystoscopy with ureter catheterization and pelvic lavage with a solution of warm sodium bicarbonate should be undertaken when crystalluria is present and seems to be a possible cause of obstruction. Alkalinization of the urine with large doses of sodium bicarbonate by mouth is likewise a

rational procedure when crystalluria is present, and seems to have been of distinct benefit in other cases in which crystals played no part. Short wave diathermy to the kidneys has appeared to be a useful adjuvant in several of our cases. We have used caffeine as a diuretic but can offer no valid conclusions as to its usefulness. Certainly, we believe that on theoretical grounds diuretics which might possibly have a toxic action on the kidneys are contra-indicated.

REGRESSION OF LYMPH NODE METASTASES AFTER ORCHECTOMY AND STILBESTROL IN CARCINOMA OF THE PROSTATE

REPORT OF A CASE

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It is not our purpose to discuss the biochemical and clinical aspects of the treatment of advanced carcinoma of the prostate by orchectomy and stilbestrol. This subject has received generous attention by many writers since the startling announcement of Huggins and his associates in 1941. It is sufficient at this time to say that our results with this remarkable palliative program have been highly satisfactory and that we share in the approval that has been so widely expressed. We reserve only the hope that the enthusiasm for the new therapy will not diminish the interest in radical perineal prostatectomy as a curative measure in those cases that properly invite this procedure.

The histological changes in the primary tumor and in its metastases, following the use of orchectomy and stilbestrol, have been described less often thus far and it is for this reason that we present this brief report. Schenker, Burns and Kahle, in 1942, published their studies of six cases of metastatic carcinoma treated with diethylstilbestrol and diethylstilbestrol diproprionate. In every instance, definite regression was noted in the nucleus and cytoplasm of the tumor cells.

CASE REPORT

An American salesman, married, aged fifty-one (Hospital No. 20,-745), was admitted to the Pondville Hospital outpatient Department September 17, 1942, complaining of backache. Six months before, after a fall, he began to suffer pain in the lower region of his back. Strapping was applied by a physician but the pain persisted and it was accentuated by coughing or sneezing. Three or four weeks before coming to the hospital, a mass developed in the right groin and this was followed by swelling of the right lower extremity from the ankle to the thigh. There was no loss of weight. Except for nocturia, three to four times, there were no urinary difficulties and there had been no recent change in the history so far as the bladder was concerned. There was a slight cough but no other symptoms were reported. The patient used alcohol

regularly in rather large amounts. Previous infection of the genital tract was denied.

The first examination in the outpatient clinic found a group of four or five large, hard, discrete lymph nodes in the right supraclavicular region, the largest measuring about 2.5 cm. in diameter. Enlarged nodes could be felt also in the right inguinal region but these could not be felt so distinctly because of a thick layer of adipose tissue overlying them. Tenderness was noted over the upper lumbar vertebrae and along the tenth and eleventh ribs on the left side. There was marked swelling of the right leg. A firm nodule in the left lobe of the prostate was found on rectal examination and additional nodules were reported in the hollow of the sacrum. The diagnosis of carcinoma of the prostate was made and the question raised of a possible separate process, perhaps a lymphoma. Hospital admission was recommended.

The first examination in the outpatient clinic found a group of four was as follows: The urine was acid, 1.021; albumin, slight trace; sugar, absent; sediment, an average of 10 red blood cells and 10 white blood cells per high power field. The blood Hinton was negative. The white blood count was 8,900. Red blood count, 4,200,000; hemoglobin, 12.2 gm. or 78 per cent. The differential count was normal. The serum acid phosphatase was 0.5 Bodansky units.

X-ray Report: Examination of the pelvis showed no definite evidence of malignant disease. There was abnormality, however, in the fourth lumbar vertebra. The density of the bone was slightly increased and in the anterior view along the right side, there was a mottled appearance. There was also very slight narrowing of the body of the vertebra on that side. No other change was found in the bones of the lumbar spine. The chest film showed a normal outline of the diaphragm. There was prominence of all the lung markings and there was definite enlargement of the hilus shadows. The aorta was dilated but there was no significant increase in the size of the heart. Enlarged hilus and mediastinal glands appeared to be present. *Conclusion:* The change in the fourth lumbar vertebra could have been due to lymphoma or metastasis from the prostate. The film of the chest was also consistent with lymphoma although metastatic disease could be excluded.

A gland was removed for biopsy from the right supraclavicular area on October 13, 1942. *Pathological report:* Study of the specimen showed an oval smooth encapsulated nodule about 2.5 by 1.5 by 1.5 cm. On the cut surface there appeared four closely packed nodes with thin capsules all filled with moderately firm, red-gray homogeneous tissue. *Microscopic:* The nodes were nearly completely replaced by masses of immature epithelial cells. These were for the most part large clear cells, with round or oval vesicular nuclei containing several prominent nucleoli. Mitoses were frequent. The cytoplasm stained poorly. The cells were tightly packed into large masses or alveolar groups with scattered, well-formed acinic lumina in the central portion. Many clumps lay in dilated lymphoid sinuses and two were present in

large blood vessels. *Diagnosis:* Metastatic adenocarcinoma, not typical of carcinoma of the prostate, pharyngeal carcinoma.

The patient was first seen in urological consultation on October 21. On rectal examination we found induration in the prostate and the left lobe was particularly firm and fixed. Rectal palpation alone, however, did not warrant a positive diagnosis of malignant disease. A cystoscopic examination was made under spinal anesthesia. The cystoscope was

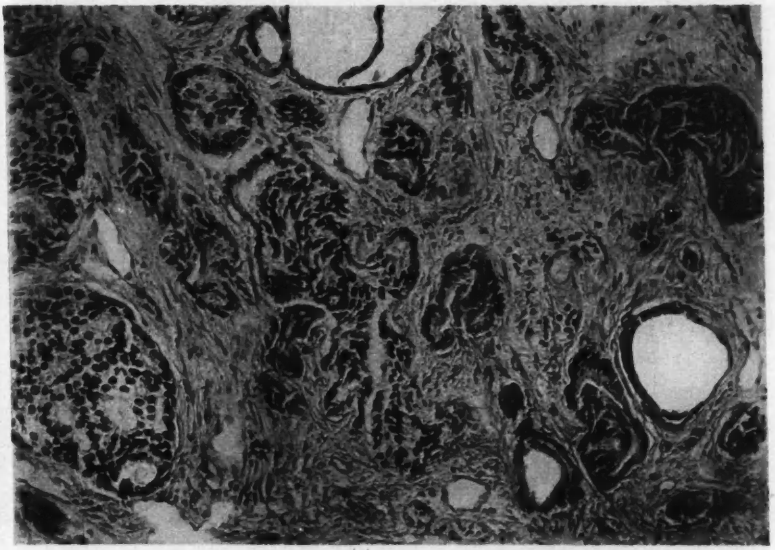

Fig. 1. Showing primary prostatic carcinoma of anaplastic type. There is some distortion of tissue from heat of high-frequency loop.

introduced with some difficulty because of marked rigidity in the region of the vesical neck. There was no neoplasm to be seen at the outlet of the bladder or in the deep urethra. There was some encroachment by the prostate but no significant obstruction except for a moderately large pale median bar.

With the transurethral resectoscope, two segments of tissue were removed from the prostate posteriorly. Frozen section examination of this tissue found carcinoma resembling somewhat the tumor found in the gland of the neck and not typical of primary prostatic carcinoma. Rectally, under anesthesia, the prostate was firm, slightly enlarged and uneven in consistency but there were no changes on which one could base a positive diagnosis.

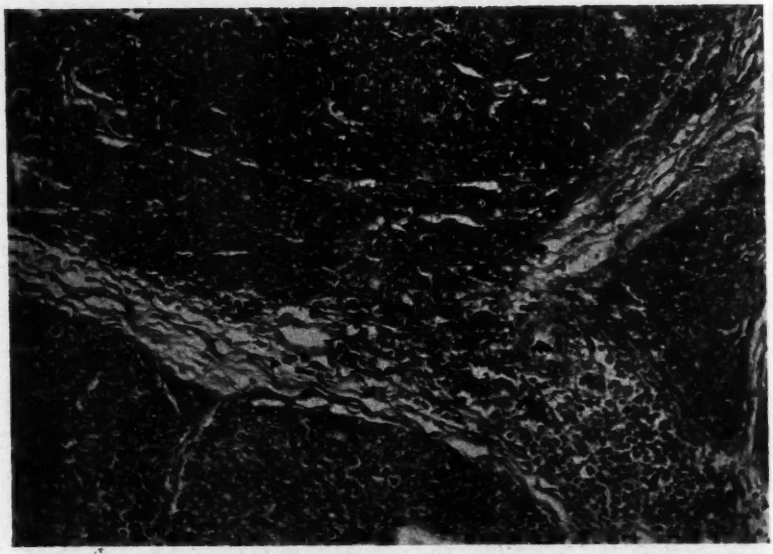

Fig. 2. Showing metastasis of undifferentiated carcinoma in cervical lymph node.

Fig. 3. Showing fibrous tissue replacing tumor in inguinal lymph node. A few scattered tumor cells persist.

The final decision was made by Dr. Shields Warren who reviewed all of the sections, including those from the supraclavicular lymph node, and identified the tumor as an adenocarcinoma of the prostate (Figs. 1, 2 and 3). His microscopic description of the prostate tissue was as follows: "Permanent sections show dilated acini packed with hyperplastic epithelium forming small closely packed alveolar structures. Invasion of the surrounding stroma is seen, as well as perineural spread. The cells are anaplastic, irregular in size and shape and show deeply staining nuclei."

On October 27, the patient reported a sudden onset of pain in the left chest and x-ray films revealed a recent fracture of the sixth rib on the left side. This appeared as a complete transverse break, with displacement, about 7 cm. from the vertebral column, probably a pathological fracture, though no signs of metastatic disease were seen in the bone in this region.

Bilateral orchectomy was performed on October 28, 1942. The testis alone was removed on each side leaving the cord and epididymis and parietal layer of the tunica vaginalis. There was no untoward reaction to this operation and the cosmetic result was excellent. The patient left the hospital with no symptoms, on November 7. *Pathological report:* The specimen consisted of two testes each 4 by 3.2 by 2.2 cm. covered by shiny, smooth, gray tunica vaginalis. On section each bulges and shows the normal, soft, bright yellow structure. *Microscopic:* The tubules showed excellent spermatogenesis with many mitoses in the spermatocytes and numerous spermatozoa.

At the first outpatient visit, about four weeks after his discharge from the hospital, the patient stated that he had gained 10 pounds. He had returned to work. His only discomfort was caused by the swelling of his right leg. Examination found definite regression of the glands in the neck and in the right groin. Stilbestrol was prescribed, 1 mg. every other day. One month later, the general condition was described as highly satisfactory except for the edema of the leg. The glands in the groin had subsided markedly; no nodes could be felt in the supraclavicular area. The dosage of stilbestrol was increased to 1 mg. daily.

February 20, 1943, about four months after orchectomy and when stilbestrol had been given in small amounts for nearly twelve weeks, a lymph node was removed for biopsy from the right inguinal region. It had been planned at the same time to excise one of the previously enlarged cervical nodes for comparison with the gland removed prior to orchectomy, but careful palpation failed to find any evidence of enlarged nodes in the neck. *Pathological report:* The specimen consisted of a rounded moderately firm elastic piece of pale gray tissue about 1 by 0.8 by 0.6 cm. On cut surface, it was shiny, firm and mottled with gray and bright yellow. No clear capsule was evident. *Microscopic:* Much of the node was replaced by dense but rather edematous connective tissue containing numerous small capillaries. Scattered in this stroma were about a dozen islands of epithelial cells with large nuclei

and scanty but clear cytoplasm. These formed solid masses or occasionally good acini. A few showed pyknosis and disintegration of cells. Occasional large cells were scattered singly in the stroma and may be epithelial in character. *Diagnosis:* Metastatic carcinoma, apparently regressing.

X-ray studies were repeated in the Outpatient Department on April 29. The previously described changes in the fourth lumbar vertebra were still present, but there appeared to be slightly less density posteriorly than in the earlier films. There had been marked improvement in the chest and the chest film was reported to be normal.

At the last outpatient visit, May 26, 1943, the patient stated that he felt perfectly well. He was driving a car regularly as a salesman and working in a Victory garden besides. His weight was 180 pounds—a gain of nearly 20 pounds since leaving the hospital after orchectomy. The swelling of the right lower extremity had disappeared except for edema of the foot. On rectal examination the prostate showed marked regression. It was described as small and soft and resembling early benign hypertrophy.

COMMENT

It seems highly probable that the clinical difficulties of diagnosis in this case, as far as the rectal examination was concerned, were related to the uncommon type of prostatic tumor that was present. It was very cellular and anaplastic and had but little stroma. It was highly malignant and the sections showed blood-vessel invasion which is rare in carcinoma of the prostate.

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INTRAVENOUS UROKYMOGRAPHY

A PRELIMINARY REPORT

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If we define an intravenous urographic film as a space picture at any definite instant of time, then a kymogram is a time picture of definite points of space. By comparing the repeated space or morphological pictures of a complete urogram we can indirectly evaluate the dynamics of the upper urinary tract. A urokymogram, however, records on one film the actual movement of definite points of the urinary tract through thirty seconds of time and so depicts the actual dynamic function.

The original conception of kymography dates from 1911 when Bronislaw Sabat[4] published a report on a new method to visualize the movement of the diaphragm, heart and aorta. In 1915, A. W. Crane[1] applied the kymographic principle to the investigation of heart disease. No great clinical interest was paid to kymography, however, until 1931 when Pleikart Stumpf[5] introduced multiple-slit kymography into clinical medicine. The first multiple-slit kymograph was made by Stumpf in 1928.[6] By 1931, he had established its clinical value. I. S. Hirsch,[2] in 1934, was the first in this country to use multiple-slit kymography for the study of heart disease, and it was his work that stimulated many others to use this method.

Multiple-slit kymography was applied to the urinary tract in 1934 by Holland, Sack and Wullenweber.[3] They called the method urokymography. In order to give sufficient contrast for the urokymogram, retrograde filling of the urinary tract was necessary. Only occasionally could a urokymographic study be accomplished following the intravenous injection of a contrast substance.

In order to eliminate completely any physiological handicaps, a readable urokymogram should not depend on retrograde injection of the contrast substance. For the past eighteen months we have collaborated with our x-ray department in trying to devise a technique of intravenous urokymography. An improved kymograph has been

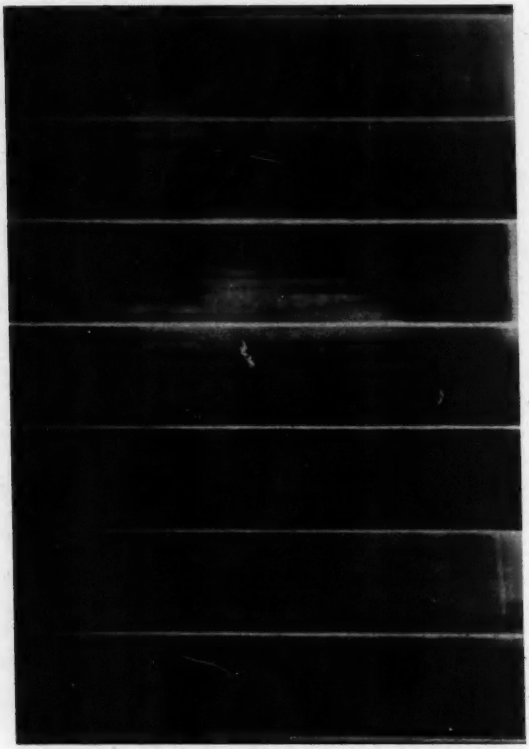

Fig. 1. Urokymogram of pelvis and upper ureter showing normal dynamic function. Five contraction waves can be seen in each kymographic segment. Horizontal white lines are unexposed portions of the film. In this manner the segments are separated from each other and actual measurements of peristaltic velocity and dynamic pattern can be made.

used with our physicist constantly checking on it and making it more efficient each time.

We have been able to obtain satisfactory intravenous urokymograms by increasing the amount of diodrast or neo-iopax injected from 20 to 30 c.c., and by keeping the patient in the Trendelenburg position for fifteen minutes. Just before the kymogram is done,

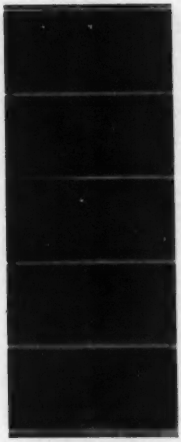

Fig. 2. Urokymogram showing normal ureteral function. Each segment shows four to five contraction waves.

the patient is changed to the flat position. By this technique a readable intravenous urokymogram can be expected in all cases in which the contrast filling of the urinary tract has been good in the ordinary urogram.

The actual procedure of urokymography is relatively simple. The most essential part of the kymograph is the "grid," which is a large lead sheet in which narrow, horizontal slits are cut 12 mm. apart, each slit being 0.4 mm. in width. In the improved kymograph which we are using this "grid" is stationary. Behind the grid is placed the film cassette, which moves downward during the single continuous exposure of thirty seconds. During this thirty seconds' exposure, the film cassette actually moves 12 mm., which is the distance between each grid slit. In order to separate these portions of the film from each other, it is necessary to have a small portion unexposed, so the x-ray exposure is automatically stopped just before the film cassette reaches the 12 mm. distance. Actually there remains 0.2 mm. of unexposed film, which, of course, shows up as a series of white lines running horizontally across the developed film. Each exposed portion of the film is therefore 11.8 mm. wide and *each of these sections represents the continuous visualization,*

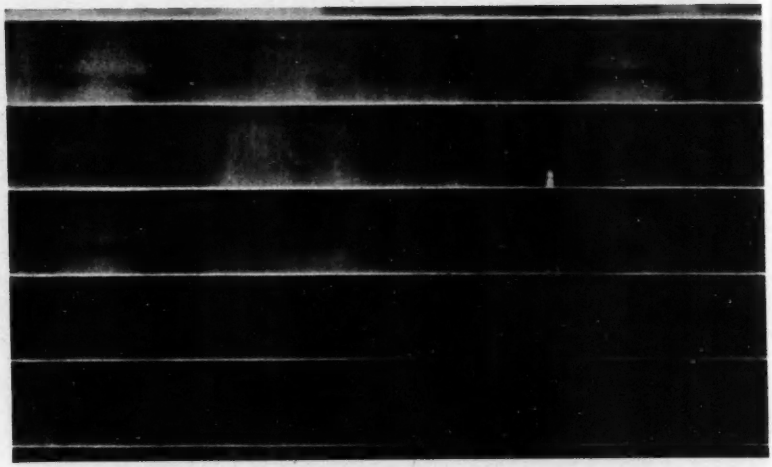

Fig. 3. Urokymogram in a case of bladder carcinoma in which both ureters show evidence of obstruction. Ureteral dynamic function, however, is still present. The dynamic pattern, however, shows two to three contraction waves in each segment.

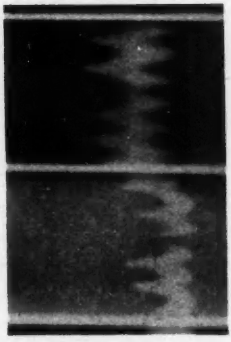

Fig. 4. Hyperperistaltis of the ureter above a slight ureteral obstruction. Seven to eight contraction waves are present but this was not sufficient to produce any symptoms.

through thirty seconds of time, of a fixed point in the urinary tract. The "fixed point" of each kymographic section is that portion of the renal pelvis or ureter which has been selected by the slit in the

fixed stationary grid for continuous x-ray exposure. We can see, therefore, that a urokymogram is, in fact, a time picture (thirty seconds) of definite points of space (each point in the urinary tract having a measurement of .4 mm. and being 12 mm. apart as determined by the stationary grid).

The actual x-ray exposure is made by a high capacity, rotating anode tube. The film target distance is 30 inches. Twenty-five milliamperes is used and the kilovoltage varies from 60 to 100. One millimeter of aluminum is used as a filter and the exposure is, of course, a continuous one for thirty seconds.

The preparation of the patient for the urokymogram is the same as that for the ordinary urogram. The patient should be instructed to hold his breath for the thirty seconds' exposure. This is usually not a difficult thing to do provided the patient tries it once or twice before the exposure is made. He is instructed, however, that if he cannot hold his breath for this length of time, he breathe in a most shallow manner so that abdominal wall movement or respiratory movement of the kidney be reduced to the minimum. All respiratory excursions are recorded on the kymogram but there is no difficulty whatsoever in distinguishing these movements which, of course, occur in every section of the kymogram, from the actual dynamic movement of the urinary tract itself.

In this preliminary report we wish to show some of the intravenous urokymograms obtained, merely to present this new method of investigation without attempting to delineate its clinical importance (Figs. 1 to 4).

SUMMARY

A preliminary report is made on intravenous urokymography, a method which permits us to more accurately study the dynamics of the upper urinary tract.

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DISCUSSION

DR. REED M. NESBIT (Ann Arbor, Mich.): I want to discuss Dr. Graves' very interesting paper. A year ago Cummings and I at the American Medical Association reported seventy-five cases of carcinoma, advanced carcinoma of the prostate, treated by orchectomy. We are at the present time accumulating data on this same group of cases which we expect to report within a month. We intend to accumulate data annually on this same series of seventy-five cases, as long as any of the patients live, and hope to report annually on that series.

A year ago in that series of seventy-five cases, we observed that there were 20 per cent immediate failures and 40 per cent failures at the time of our report. We have incomplete data at the present time, but it now appears that there is an additional probable 30 per cent of failures, what we call delayed failures, and at the present time in that series there is probably a 60 per cent failure in the total series, although there may be more. I wish to submit this thought to you, which has occurred to us: If, as seems likely, we have in the hormone management of carcinoma of the prostate advanced something which at least is favorable in perhaps only 50 per cent of cases for a year or more, I wonder if perhaps we might be well advised to save our trumps until it is necessary to play them in this type of case. In other words, perhaps we would be well advised not to institute hormonal therapy, either orchectomy or administration of estrogens, until the patient develops symptoms of far advanced cancer of the prostate. I submit that to you for thought and would appreciate discussion of it, if that is appropriate, at this time.

DR. BARRINGER: May I ask you one question? How many apparent total cures have you got of the seventy-five cases?

DR. NESBIT: I don't know of any.

DR. BARRINGER: You don't know of any. I mean symptomatically.

DR. NESBIT: I don't suspect there are going to be any cures in that particular series of seventy-five cases as we are following them.

DR. ORMOND: Reed, what do you mean by failure?

DR. NESBIT: I mean by failure this: Immediate failures were 20 per cent in that series. In other words, orchectomy produced no change whatever in symptoms or signs or chemistry. By delayed failure I mean the patient who becomes clinically improved after orchectomy and at some subsequent time becomes a backslider and re-develops his symptoms and eventually goes on and dies of his cancer. We have observed in the series reported a year ago that we had one patient who was a delayed failure after seventeen months. We had another patient who was a delayed failure after twenty-two months. We are observing now delayed failures after a period of three years. If we perhaps can give relief of symptoms for a period of eight months, why not delay the institution of that therapy until the man needs it, and, as I said before, play the trumps when we need to take tricks with them.

DR. YOUNG: Let me ask you a question. What effect does it have as far as you can make out, on obstruction to urination?

DR. NESBIT: We have observed several cases in which, for various reasons, we could not operate upon the patient in whom we instituted hormone therapy, where a very marked relief of urinary obstruction occurred. Five of our patients up to the present time have been put on suprapubic drainage. In four of those five cases, we have subsequently removed the suprapubic tube, but they may be due to a diminution in edema, and so forth. But I have observed this in a number of cases where there was far advanced cancer with a fairly high degree of obstruction, simply institution of hormone therapy of one type or another has relieved the obstructive symptoms. We have had some cases in which all evidence of primary neoplasm has disappeared, and the patient has gone on and had an advance in metastases. Of course, everybody has observed that.

DR. YOUNG: Another question. Suppose a person comes in with a large residuum or almost complete retention and big carcinoma, and so forth; do you do an operation to relieve the obstruction first, or do you do the orchidectomy first, or do you do them simultaneously?

DR. NESBIT: On the basis of our own experience, this is what

we are now doing: If the patient has a very large, far advanced carcinoma, we are not doing a transurethral resection for this reason: we have had some very disappointing results from transurethral resection in massive carcinoma. It is a difficult operation to perform effectively. The patient is very apt, if you perform an adequate resection so as to give him an adequate relief of obstruction, to be incontinent. So, in massive carcinoma of the prostate that requires drainage, we provide it by suprapubic drainage or catheter. We have put three or four patients of that type that you refer to on catheter drainage and have instituted hormone therapy, either orchectomy or estrogenic therapy, and then at a subsequent time have removed the catheter. In all cases in which we have instituted urethral catheter drainage augmented by the other therapy, we have been surprised to find that those patients have been relieved of their obstruction at least temporarily and have been able to urinate.

DR. KEYES: You say all but one?

DR. NESBIT: No, the suprapubic ones.

DR. BARRINGER: Just what is your theory behind waiting until they get bad?

DR. NESBIT: All right, I am a patient, and I have an advanced cancer, and I know it. I have no pain from metastases, and I have plus or minus obstruction. Let's say I have obstruction that can be relieved by resectoscopy. Now I don't want to have the door slammed in my face; that is, I don't want to use whatever possible relief I might eventually get from the use of hormones by taking it now. What is the object of taking it now? If I don't have any symptoms now, why take it? It is symptomatic relief we are producing.

DR. BARRINGER: I thought the object was taking it now. I rather believe there are a certain number of these patients that, as far as we can see, are well, perhaps 10 per cent, something like that.

DR. GEORGE G. SMITH (Boston, Mass.): The question that Dr. Nesbit has raised about the time at which hormonal therapy should be instituted has been brought up in connection with total perineal prostatectomy for cancer. I had quite a discussion of that point

with one of the men on the staff at the Massachusetts General, who maintained that the testes should be removed at the time of radical perineal prostatectomy. I disagreed with him, because it seemed to me that the recurrence of these malignant prostates must mean one of two things, either the cancer cell has adapted itself to live with a new hormonal situation or else more hormones have been provided by some change in the hormonal production in the body. Possibly the adrenals, which we know produce androgens, may have increased their output. This is pure supposition, and I am sure Dr. Cahill and some of the other men who have studied the hormonal output can give definite facts on these points.

In discussing the interesting paper on sulfonamides, I would like to say that at the Massachusetts General Dr. Maisel, resident in pathology, has done some very good work on the production of casts in the kidney tubules following sulfonamide therapy. He has done a lot of animal experimentation. In a patient I had who died after a complex illness some three or four weeks after she had a very moderate course of sulfonamides, he was able to demonstrate the presence of these casts in the tubules. The casts ulcerate through the wall of the tubules and get into the interstitial tissue and set up an inflammatory reaction. That is not new. Other men have reported the same thing in tuberculous nephritis due to the crush injuries in which myohemoglobin casts are formed and probably in transfusion nephritis as well. The symptom complex seems to be a fairly definite one and more or less similar in all three types.

Dr. John K. Ormond (Detroit, Mich.): It was in connection with Dr. Nesbit's remarks on the treatment by orchectomy that I want to mention a patient who, I think, was the first on whom we performed orchectomy, back in February, 1942. A conservative perineal prostatectomy had been done on this patient and carcinoma was found. Immediately orchectomy was performed. He gained weight, went back to work and worked until this last March, when he began to go downhill. But the striking thing about it was that, although he went downhill gradually, he was suffering no pain till recently.

Dr. Clyde L. Deming (New Haven, Conn.): I would like to discuss the first two papers. The problem of anuria following sulfa drugs is undoubtedly laid in our laps. There is an attempt on the

part of research laboratories and many clinical men to find a drug of sulfa compounds which will not produce anuria. I would like to report a case of sulfamerazine anuria.

A young man twenty-two years of age was admitted to the New Haven Hospital last month with pyogenic meningitis. No organisms were ever found in the spinal fluid. On the first day he was given 8 grams of sulfamerazine and on the second day 6 grams. On the third day, his blood level of sulfa was 8.4 grams. On the third day he put out only 300 c.c. of urine. On the fourth day he put out but 100 c.c. On the fifth day, he was completely anuric. Cystoscopic examination showed that he had a plug of acetyl crystals in his lower right ureter and that the left ureter was nonfunctioning. The pyelogram on the left showed that the upper ureter and pelvis were serrated in outline, indicating that the left pelvis was filled with crystals. In other words, this man had an obstruction to his lower right ureter and a complete obstruction to his upper left ureter, so that it was a case truly of sulfamerazine anuria.

He was relieved by catheterization of both ureters and irrigation of the pelves with alkaline solution.

With regard to carcinoma of the prostate and castration, I would like to say that in our experience we have had two cases who have not been relieved of pain. Both of those cases have been cases where the carcinoma has grown forward, involving the bulb, giving both patients constant erections. Those patients have not been relieved by castration nor by stilbestrol.

I would like to compliment Dr. Hughes upon his presentation.

DR. GEORGE F. CAHILL: I am inclined to differ with Dr. Nesbit in respect to time of orchectomy and prostatic carcinoma. Recession of these tumors sometimes occurs with orchectomy in cases without bone symptoms or signs. Therapy is still ahead of biological explanations concerning many factors. Some of these patients, later on, develop positive Aschheim-Zondek tests after orchectomy. We wonder, therefore, whether the adrenal with the pituitary takes on some of the testicular function. Many symptomless patients will show marked improvement in their nutrition and general activity after orchectomy.

Since all the steps are not yet explained, at least the therapeutic value of orchectomy and hormonal treatment has been established.

DR. WILLIAM P. HERBST, JR. (Washington, D. C.): I think

the problem of the prostatic malignancy revolves mostly around the chemistry of it. The more we get into the chemistry of it up to the present time, the more confused we become, the more unable we are to explain many individual observations which we make upon any theory which we wish to propound.

I have a feeling very definitely that orchectomy and administration of these various steroid compounds is very different in some respects. I don't know what they are, but I think they are different and I think eventually we will find that they are different. I think that Dr. Nesbit's point is very well taken. The reason I feel that it is, is this: Our bodies resent disturbance of certain biochemical levels or phases. When we disturb them, either by removing substances or putting substances in them, there is something that automatically attempts to resume the level as it was before we interfered with it. This being true, it seems to me that if we can keep the patient comfortable, allow him to void, let's appreciate that state as long as we can and then go into the phase of upsetting the biochemistry with the hope that we will have that much additional life expectancy.

Certain of the biochemical estimations which have been made and which have already been put forward definitely indicating the clinical course in these cases do not hold in many individual cases.

I was most interested in the paper on urokymography. I didn't understand it and I would like to ask what was the period of exposure in the individual exposures that were made during the pictures that we saw on the screen. The reason I ask that is this, that the rate of motility in the urinary tract is quite variable and if the exposure is long enough, we cannot get, you might say, a snapshot picture of the motility at any one time. I am very interested to know the answer to that.

DR. C. D. CREEVY (Minneapolis, Minn.): I would like to make just one or two points. In the first place, I think Dr. Hughes ought to be congratulated very warmly on presenting what appears to be the only method which permits one to study the motility of the intact, undisturbed human ureter. Every other method I have heard of involves doing something to the ureter itself. This method does not, and it ought to permit the accurate evaluation of the effects of many drugs on the ureter. That information ought to be very useful clinically.

The other point that I wanted to mention was (I think Dr. Herbst has already covered it) Dr. Nesbit's feeling that the period during which the good effect of hormone therapy on carcinoma of the prostate will last is limited in duration.

Most of the patients with carcinoma of the prostate, at the time of admission, do not have any pain. They come in with urinary complaints. If one can relieve them with transurethral resection and save the hormone therapy until later, the total period of comfort for that patient may be much greater than if one employed the hormone therapy at the start and let it wear itself out before the pain would have begun without it.

We have seen a patient with anuria from sulfamerazine at the University Hospital. It was discovered later that the patient had been receiving ammonium chloride as an expectorant, so that the pH of her urine was 4.5 at the time when the administration of sulfamerazine was begun. This accounts very satisfactorily for what happened.

DR. WILLIAM F. BRAASCH (Rochester, Minn.): Dr. Hughes' very interesting contribution would seem to open up many avenues for investigation in the field of ureteral physiology. It should be of practical aid in enabling us to differentiate between dynamic and adynamic ureterectasis. It is frequently very difficult to differentiate between these two conditions.

In regard to the anuria following use of the sulfonamides, I was rather interested in the high dosage which had been employed in the cases cited. From 4 to 6 grams had often been administered. This is much higher than we employ in the treatment of urinary infection. I have often observed that patients who have been treated with sulfonamide drugs before coming to the Clinic had been given much larger amounts of the drugs than we are accustomed to prescribe. We find that the same results may be secured with 2 or 3 grams daily. This was brought out in the experimental work of Helmholz and has been substantiated by wide clinical experience. I don't remember ever having seen anuria following the use of sulfonamides in the dosage we employ. Although the daily urinary output is carefully watched and the other precautions against drug idiosyncrasy are taken, it would seem that low dosage is the most important factor in that we do not see anuria following the use of sulfonamides.

DR. CAHILL: May I ask a question? I want to ask, among the men here, how many sulfonamide anurias developed in the urologic department?

DR. LEON HERMAN: I think that something should be said about the influence of the cystologic type of prostatic carcinoma in relation to the effect of orchidectomy. In a recent paper Dr. Huggins reported an unusual proportion of anaplastic carcinomata, and in these orchectomy apparently had no beneficial effect. Anaplastic carcinoma of the prostate in our experience is exceedingly rare. In fact, I can recall only one case and this patient has been benefited enormously by orchectomy.

DR. CAHILL: I agree with you.

DR. HERMAN: Perhaps it might be worth while to describe the case.

The patient had a large, smooth, firm tumor confined to the right lobe of the prostate. The correct diagnosis was not made. The complete suprapubic enucleation of the mass proved impossible. A capsule containing 100 mg. of radium was placed in a Hagnar bag and the latter pulled into the prostatic bed. In this manner 2400 mg. hours of irradiation were given and supplemented by deep x-ray therapy. The patient voided well eventually but refused to discard the suprapubic tube. One year later the patient returned complaining of pain in the right shoulder and neck. Examination disclosed metastases to the acromion process of the right scapula, cervical spine and ischium. Orchectomy was then done. The metastases disappeared with the exception of small areas in the ischium. The patient, sixteen months after operation, is entirely without symptoms; this is one of the best results, if not the best, that I have observed.

I agree with Dr. Nesbit that orchectomy, being a palliative measure, should be reserved for that time when palliation is essential; this is obviously in the late stages of prostatic carcinoma.

DR. JAMES C. MCCLELLAND (Toronto, Canada): Just one word. In our clinic, we have been accustomed to using small dosages. It is 2 and 3 grams per day, and this dosage has not continued longer than four or five days—five days maximum. So it is a small dosage.

To answer Dr. Cahill's question, in our department I have never seen an anuria develop from these small dosages.

DR. JOHN K. ORMOND: We have had one case of anuria in the urological department. That was the patient in my report in which the drug had been given as a prophylactic before resection and after resection was given again. That patient developed anuria and died. Now, unfortunately, we did not have an autopsy, so there still may be some question as to whether it was the drug or whether it was something else, but we attributed it to the drug.

DR. BARRINGER: How much did he get each day?

DR. ORMOND: He was getting 4 grams. Our regular dosage has been between 2 and 4 grams a day, keeping it up as long as six days. This is the only case in which we have had any trouble.

DR. BOLAND HUGHES (Philadelphia, Pa.): To answer Dr. Herbst's question, the time exposure is thirty seconds on the urokymogram.

DR. HERBST: Is that constant, kept on thirty seconds?

DR. HUGHES: Oh, yes; it is thirty seconds' continuous exposure.

SURGICAL TREATMENT OF ELEPHANTIASIS

HUGH H. YOUNG, M.D.

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital Baltimore, Maryland

I wish to present the history of a case and motion pictures in color† of a radical operation which I carried out.

The case was one of very extensive non-filarial elephantiasis of the scrotum in a physician aged forty-nine years (B. U. I. 32852). Twenty-three years before admission he was in an automobile accident and sustained an injury to the scrotum which necessitated removal of the left testicle. Several weeks later the operating surgeon urged to patient to allow him to inject heated paraffin into the scrotal sac in sufficient quantity to form a globular body of the size and shape of the lost testicle. Paraffin, liquified by heat, was injected, and then formed into the size and shape of the opposite testicle by digital manipulation. The immediate result was very satisfactory; the scrotal contents on both sides were about equal and normal in appearance. In a few months the paraffin mass lost its ovoid form and spread into the tissues of the right side of the scrotum, then across to the opposite side, and finally beneath the skin of the penis. After that there was a slow but gradual increase in the size of the scrotum, the tissues becoming greatly thickened and indurated.

About five years ago the scrotal mass had become very large and engulfed the penis, only the glans of which projected from the scrotal mass. After this, sexual intercourse, which had become progressively more difficult, was impossible. About three years ago he began to have dermatitis, and at times superficially ulcerated areas all over the surface of the scrotum, which in the meantime had become about eight inches in diameter. He was put on sulfapyridine, and during the year before I first saw him, he had been free from erysipelas, but the mass had continued to grow and extended backward to the perineum, upward and outward into each groin, completely covering the penis. The edematous foreskin alone projected slightly from the hard encircling mass. The condition on admission is shown in Figures 1 and 2. I realized that I was dealing with a huge irregular indurated mass which had invaded the suprapubic region, both groins, the entire surface of the scrotum and the tissues as far back as the perineum.

It was evident that in order to effect a cure, it would be necessary to carry the incisions outside the indurated mass, which was to be removed in one piece with the exception of the inverted foreskin that I had decided to preserve to cover the penis (Fig. 3). The upper incision started at the antero-superior spine on the right side, curved down-

†The motion picture was taken by Mr. William P. Didusch.

Fig. 1. Showing irregular, greatly indurated skin up to a point 10 cm. above the shaft of the penis and outward along the right groin for a distance of 20 cm., and along the left groin for 13 cm. The induration extends posteriorly almost to the perineum, a distance of 14 cm. from the penis.

Fig. 2. Left oblique view showing the bulging elephantoid scrotal mass with the foreskin projecting slightly from the cavity in which the penis had disappeared.

Fig. 3. Showing the penis retracted forcibly with the foreskin, which itself showed no evidence of induration.

ward across the lower portion of the abdomen at a point about three or four centimeters above the symphysis pubis and next to the left antero-superior spine. An external incision was then made, commencing near the end of the inguinal incision, and diverging from it as it passed down the groin, then around the side of the scrotum, just external to

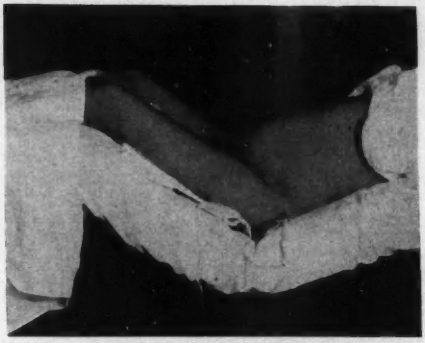

Fig. 4. Showing position in which patient was placed on his return to ward to prevent strain on the lines of sutures.

the edge of the subcutaneous induration. This incision swept around behind the scrotum, through the anterior part of the perineum. At this point it went through the indurated tissues, as it seemed inadvisable to excise all the pathological tissues in the perineum. The same incision then swept around the left side of the scrotum external to the line of induration and up along the right groin to join the abdominal incision two or three centimeters away from the antero-superior spine. The superior incision was then carried down through the skin, subcutaneous fat and superficial fascia until the deep fascia covering the lower abdominal muscles was reached. By blunt dissection the mass was stripped away from these muscles and from the fasciæ of the groins. Finally, in the midline the suspensory ligament and root of the penis were disclosed. The left lateral scrotal incision was carried through skin, fat and fascia until the tissues posterior to the elephantoid mass were reached. The same thing was carried out posteriorly except that the incision went through the indurated tissues in the perineum.

Dr. Hugh J. Jewett then came in to assist me, and continued the dissection on the right side similar to that which I had done on the left.

I then made an incision in the midline anteriorly from the abdominal incision, through the indurated tissues down to the opening from which the edematous prepuce and penis projected. The scalpel passed through

moderately indurated tissue about three centimeters thick before finally the body of the penis was reached. The mass was separated from the shaft of the penis on each side, exposing the suspensory ligament and Buck's fascia that surrounded the corpora which were not involved in the pathological process. An incision was then made through the retroverted prepuce at a point where it joined the indurated skin. The penis was then lifted out from the scrotal mass. The outer portion of the penis for a distance of about seven centimeters was covered by the inverted, non-indurated foreskin. The root of the penis and the suspensory ligament were uncovered. In this dissection the spermatic cord which remained after the castration (this had been done at the time of the accident) was uncovered, was divided close to the external ring and ligated.

On the right side Doctor Jewett busied himself with isolation of the right spermatic cord and followed it down behind the indurated mass and freed the testicle, epididymis and tunica vaginalis from the tightly adherent, indurated mass of tissue.

This having been accomplished, the huge indurated mass, freed from the deeper tissues and from the penis, was lifted out. This left a great cavity in which lay the penis and the bulbous urethra. Colles' fascia had come away with the indurated scrotal mass. Examination showed that the excision of indurated skin and subcutaneous tissues had been complete everywhere except posteriorly, where some of the remaining indurated tissues were removed with scissors.

By loosening the skin on the inner side of the thighs and above the groins and suprapubic region, it was found possible to cover a large part of the wound. Fortunately, most of the shaft of the penis was already covered by the inner layer of foreskin which had been preserved. To cover the shaft of the penis back of that, it was possible to draw tissues loose from the groin on each side, and these were held together with silver wire sutures. For the undersurface of the shaft of the penis above the inverted sheath of foreskin, it was found possible to take a flap from the scrotal skin of the left side to cover about two and one-half centimeters of the undersurface of the penis. Before finally closing the scrotum a pocket was made for the right testicle which was then drawn downward and placed in this pocket to the right of the median line. The wounds were then closed with drainage. Plain catgut was used in places to approximate the subcutaneous fat and fascia and deep through-and-through sutures of silver wire to approximate the skin and subcutaneous tissues. All bleeding had been carefully arrested by clamping and ligating or fulguration. Powdered sulfanilamide was sprinkled well over the wound before closure. The patient stood the operation well.

On his return to the ward, he was placed in bed with the back and thighs elevated (Fig. 4). In this way strain was taken off the lines of suture. As a result, the wound healed *per primam*, except in places where it had been drained. Convalescence was satisfactory. When the patient left the hospital, four and a half weeks after the operation,

the penis and scrotum were of almost normal proportions, and only a little induration of the tissues in the perineum remained.

A year after operation the patient reported that intercourse was entirely satisfactory and ejaculations not precocious.

Fig. 5. Conditions present sixteen months after operation. The penis is of normal size and length, and for the most part covered with an elastic integument, which previously had been the interior of the foreskin. There was only slight induration at the peno-scrotal junction.

On March 7, 1944 (sixteen months after operation) the patient reported for a check-up. The conditions present are shown in Figure 5. As seen here, the penis was of normal size and length, and for the most part covered with an elastic integument, which previously had been the interior of the foreskin. There was only slight induration at the peno-scrotal junction. The patient stated that erections were excellent and normal in every respect, and intercourse very satisfactory. There was a deep, curved scar that went from one anterior-superior spine to the other, and also scars that ran around the base of the penis and the scrotum, which was about normal in size and contained, on the right side, a mass that was evidently the right testicle surrounded by a good deal of scar tissue. There was no recurrence of the elephantiasis. There was no ulceration anywhere and no tenderness or pain. On rectal examination the prostate and seminal vesicles were distinctly smaller than normal. The patient voided urine with a good stream; urinalysis was negative.

PSEUDO-ELEPHANTIASIS OF THE SCROTUM

REPORT OF A CASE

GEORGE R. LIVERMORE, M.D.

Memphis, Tennessee

Pseudo-elephantiasis is due to lymphangitis with blockage of the lymphatics. This results in edema, swelling, marked thickening and hypertrophy of the organ involved. In the case herewith reported, the edema and fibrous thickening were so great that the skin varied in thickness from 0.5 to 2.5 inches. The pendulous scrotum was so large, edematous and heavy that the skin would often crack and become abraded. From these cracked and abraded areas, serum would exude.

The etiology of pseudo-elephantiasis is rather obscure. Blockage of the lymphatics of the scrotum and penis is said to be the cause, but the etiology of the blockage is not so clear. It may be due to cicatricial contraction following chancroidal, tuberculous, and syphilitic ulcerations or trauma. These, however, are of common occurrence, while pseudo-elephantiasis is exceedingly rare.

Herman says chronic edema, or pseudo-elephantiasis, may follow the removal of inguinal lymph nodes or hernia operations, streptococcic or syphilitic lymphangitis, lymphopathia venerum and granuloma inguinale. My experience, and that of some observers, is that causes of chronic edema resulting from the removal of inguinal lymph nodes, though of long duration, finally subside under rest, hot applications, adhesive strapping, et cetera, and is a different entity from psuedo-elephantiasis.

In addition to the edema, hypertrophy, et cetera, of the part affected, rigors, fever, and sweats with leukocytosis occur at intervals due to lymphangitis.

Excision of as much of the hypertrophied and edematous tissue as possible should be made, using grafts of skin from uninvolved parts to fill in denuded portions where skin areas cannot be approximated.

CASE REPORT

O. E., a white musician, married, aged twenty-seven, was 5 feet, 10

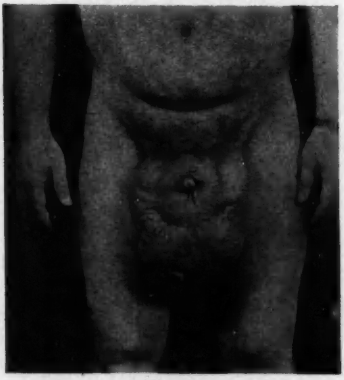

Fig. 1.

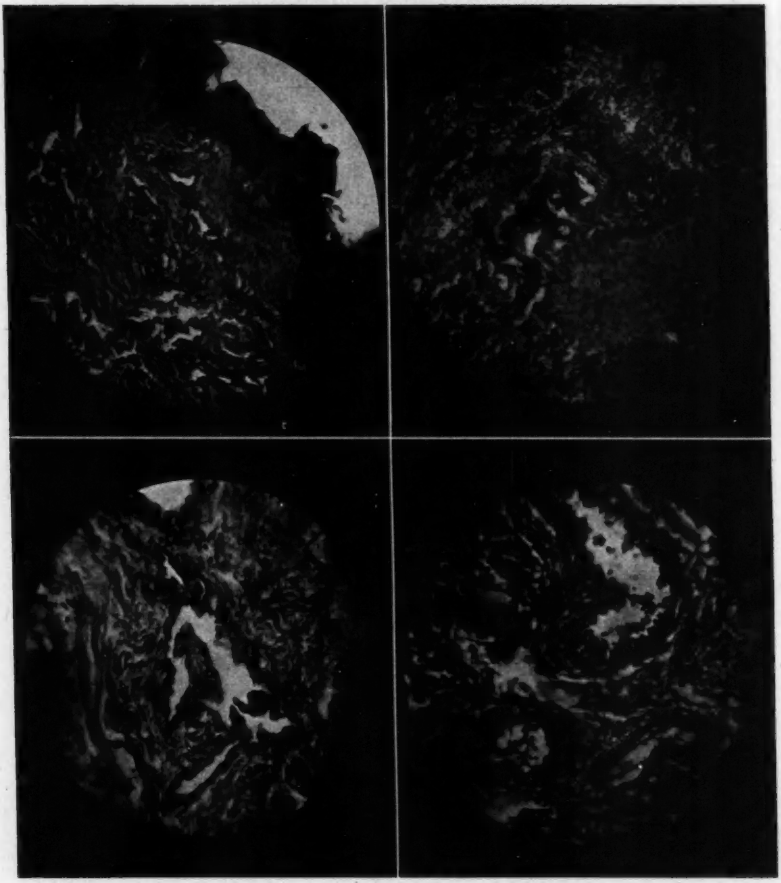

Fig. 2.

inches in height and weighed 250 pounds. His father and mother were living and well. There was no history of pseudo-elephantiasis in any other member of his family. There was no history of trauma or cicatricial contraction, and he had never had any venereal disease. He had had two recurrences of the condition (Fig. 1), and the sequence of events has been about the same in all three: gradually increasing enlargement of the scrotum over a period of two years or more; rigors, fever, and sweats at intervals of six weeks to three months; no pain

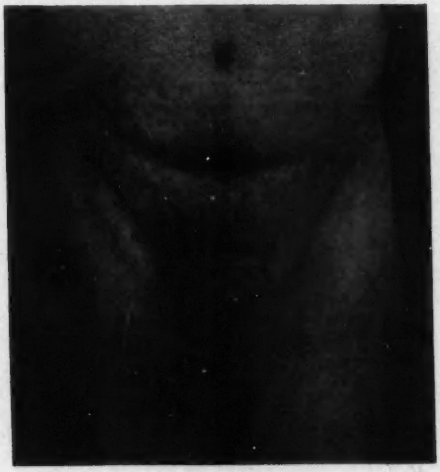

Fig. 3.

other than a sense of weight, dragging, and fatigue; sexual intercourse unsatisfactory, especially when the enlargement was great, as introduction was only partially successful.

A blood Wassermann test was negative. His red cell count was normal, and there was no leukocytosis, except when he had attacks of rigors, fever, sweats and general malaise. The blood was negative for malaria and filaria.

At the first operation May 5, 1938, the scrotum measured 15 inches in circumference and 7.5 inches in width. The second operation was done March 3, 1940, and the measurements of the scrotum were: circumference, 17 inches; width, 8 inches. At the third operation April 20, 1943, the circumference was 20.5 inches, the width 9 inches, and from the upper limit of the scrotum to the perineo-scrotal junction, 21 inches. At each operation the skin was greatly hypertrophied, cracked, abraded, and serum exuded from the abrasions. The skin varied in

thickness from 0.5 to 2.5 inches and was exceedingly vascular. The subcutaneous tissues were very edematous. At each operation, as much of the scrotum as possible was excised; in each instance, the skin of the posterior aspect of the scrotum was only slightly involved, hence this was utilized to form a new scrotum. In the first and second operations, flaps of skin were brought over from the abdomen or thigh in the hope of connecting with unblocked lymphatics, but as it had no effect, this was not done at the last operation.

The pathological specimen consisted of a large section of the scrotum which measured approximately 25 by 20 cm. and weighed 3 pounds and 4 ounces. The epidermis was markedly thickened, roughened, abraded, and showed some bluish discoloration. The cut surface was markedly edematous and had a glistening, pearly white appearance. The thickness of the specimen was about 6 cm. The fresh cut surface revealed numerous cavernous spaces filled with clear mucoid material. Other areas were composed of dense white tissue.

The histological examination was characterized by marked hypertrophy of the epidermis. There was considerable cornification. The underlying tissue was loose and edematous. There were many small, irregular channels lined with a single layer of cells which were surrounded by lymphocytes and plasma cells. In some areas the spaces were cavernous in type and were surrounded by a large number of lymphocytes. The edematous connective tissue was interspersed with muscle fibers.

Other areas presented large channels which had become partially obliterated. Collections of small lymphocytes simulated the appearance of follicles. Marked edema gave the connective tissue stroma a very fibrillar appearance. Many blood vessels were found. Diagnosis: Pheudo-elephantiasis with chronic lymphangitis. (N. F. Leake, M.D., pathologist.)

The patient made a nice recovery from each operation, and now, although the scrotum is larger than normal, he is delighted with the relief from the discomfort of carrying such a heavy organ. The last time I saw him just before coming to this meeting, he said he felt so relieved he would be willing to undergo the operation every two years for the rest of his life just to feel normal again, even for so short a time. Figure 3 shows the postoperative result.

DISCUSSION

DR. JOHN K. ORMOND: I would like to call Dr. Young's attention to a recent case that we have had, in which the problem had to be solved in a little different manner. This case will be published by Roth and Warren in a few weeks. The patient had the whole scrotal skin, except a small V-shape piece just under the penis, and the skin of the penis pulled off by a machine. He came in for repair and brought the skin with him, but it was in no condition to reapply. Dr. Roth and Dr. Warren were able to get a beautiful result by undermining the inguinal crease and bringing that over and forming a scrotum. The interesting thing is that the inguinal crease has since re-formed and formed a good scrotum. What I want to call to Dr. Young's attention is the fact that a machine graft from the thigh was used to cover the penis. That man has since had several erections. At first they were a bit painful, but the last erections have been without any difficulty whatsoever.

DR. REED M. NESBIT: Could you put Dr. Livermore's last slide on?

Dr. Livermore has pointed out that this man has had three operations and has expressed the willingness to have the same operation performed every two years from now on. I wonder if it would be possible to prevent recurrence of this pathological entity by a very simple procedure.

DR. LIVERMORE: Good! Tell us.

DR. NESBIT (Slide): I wonder, in view of the fact that apparently the lymphatics here are the things that are preventing adequate return of lymph, if one were to anastomose the scrotum to the thighs, somewhat like a first stage Torek operation, if that would give him lymphatic drainage.

DR. LIVERMORE: (Demonstrating lantern slide) The thick edge on each side is where the drainage was, through and through, from here to here. The patient had a little infection, particularly on that side, and there was some thickening and swelling there following the infection. I think when that clears up (pictures were made four weeks after the operation), the thickening will subside.

DR. NESBIT: My suggestion is to anastamose the scrotum to the thigh here, such as we do when we perform a Torek operation, then he will have drainage through his leg lymphatics.

DR. DAVID M. DAVIS: Dr. McCrea, of Philadelphia, reported a year or two ago at a local meeting the use of an oval ball of lucite for replacement of a lost testicle and it certainly was much more satisfactory than paraffin.

We have operated in a few cases of pseudo-elephantiasis like the case of Dr. Livermore and feel that the important thing is to remove all of the diseased tissue. Usually, if this is done thoroughly, and I think Dr. Young will agree, there will be no recurrence. The trouble is that usually one fails to effect complete removal because one loses courage about the extent of the denudation.

In that connection, I remember a colored man years ago in Baltimore who lost all of the skin of his penis as a result of the extravasation of urine from stricture. The penis was completely denuded, foreskin and all, right up to the glans. The glans was not denuded. We covered the penis with small pinch grafts, placing them in a very orderly fashion in rows the same distance apart. They took in really miraculous fashion. Now, of course, the pinch grafts were of black skin but as the skin grew out and joined up with the adjoining pinch grafts, the intervening parts were white, so that the organ looked like a checkerboard. Functionally it was perfect, and the patient was very proud of its appearance.

DR. GEORGE R. LIVERMORE: All I can say is that I cut and whittled and cut until all of the indurated and thickened tissue had been removed. At each operation we had quite healthy skin to use for scrotal flaps. Now I think I will have to try Reed Nesbit's suggestion, because that seems to be the best plan that I have heard to start new lymphatic drainage.

AUTOPSY TWENTY-TWO YEARS AFTER CUTANEOUS URETEROSTOMY FOR TUBERCULOSIS

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Dr. Lynn Halbert was an intern in the State Island Hospital when I was first called to see him in the autumn of 1920. He was quite ill, his fever hectic, his urine thick with pus, his micturition unbearably frequent and painful. His previous history was of tuberculosis; a costal cartilage when he was nine, a nephrectomy two years before I saw him.

After some fumbling, the details of which have been reported in the *Journal of Urology* (44:40, 1940), a cutaneous ureterostomy was done on March 21, 1921. He became immediately and completely well, and for twenty-two years thereafter his life was that of a busy and successful surgeon. He was taken ill in January, 1943. He rapidly faded during February and finally, after a week of vomiting and bowel obstruction, he died on March 6. Exploration a few hours before death revealed tuberculous peritonitis.

Autopsy revealed tuberculosis of various organs, notably the lungs, liver, spleen, kidney and peritoneum. The kidney was pyonephrotic. There was a large perinephric abscess. Death was attributed to the tuberculous peritonitis and to the renal and perirenal condition. The kidney tissue was quite destroyed. On admission the blood urea nitrogen was above 120 mg. per 100 c.c.

During the twenty-two years between ureterostomy and death the patient was in active surgical practice, apparently in vigorous health. Yet the tuberculosis in the remaining kidney persisted and got him in the end.

I submit this comment because in 1940 I reported a number of ureterostomies without catheter to illustrate how well they did, and I suggested that perhaps the operation might be found useful, chiefly, for unilateral renal infection when intractible bladder irritation persists after nephrectomy. Perhaps this was an error. Of the six cases reported, four patients have survived for more than five years. Two of these are now dead with tuberculosis in the remaining kidney (sixteen, twenty-two years), and there has been a flare-up of a

tuberculous hip in a third. It looks as though bilateral renal tuberculosis may do very well after nephrectomy and ureterostomy without catheter.

STENOSIS OF THE EXTERNAL URETHRAL MEATUS

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Stenosis of the external urethral meatus is the neglected stepchild among serious urinary tract obstructions. A study of the world's medical literature of the past twenty-five years discloses an average of one contribution a year on this subject, predominantly in German, and nearly always concerned with a single case report.[1,3,5,6,7] Its consideration in urologic and pediatric literature has been scant. Most patients in whom the lesion is recognized are children, in practically all of whom it may be considered congenital and it may also be congenital in adults. In older patients its recognition is most likely to coincide with attempted urethral instrumentation or the acquisition of gonorrhea. While the symptomatic discomfiture due to urinary difficulty immediately concerns the patient or his parents, urinary backpressure damage of the proximal urinary tract, and particularly the kidney, is the important vital consideration. Urographic study in a relatively small series of these cases may be expected to reveal examples of advanced upper tract obstructive uropathy and wholly disproportionate to the commonly accepted benignity of the meatal lesion. Despite the usual utter simplicity of diagnosis of meatal stenosis by inspection and of its treatment by meatotomy, thousands are today suffering serious progressive urinary obstruction because of the failure of their medical advisers to recognize this condition. This report is based on a clinical study of 152 personal cases in which I have satisfactory office or hospital records. Adults have not been included nor have a large number of children whose records have been inadequate. The age of the patients in this series ranges from seven weeks to sixteen years; a fourth were under twenty-four months of age; half were between twenty-four months and ten years. Twenty-six were females. The common complication of stenosis of the external meatus—the ulcerated meatus—is also considered. Unfortunately for our records, urographic studies were made in only a limited number (sixty-three, cystoscopy eighty-seven) of these patients, yet sufficient to demon-

strate beyond question the potential gravity of the tight urethral meatus.

ETIOLOGY

Etiologically stricture of the external meatus may be classified as: (1) congenital (98 per cent); (2) acquired (2 per cent), (a) traumatic (indwelling catheter, instrumentation, et cetera); (b) infection (gonorrhea, non-gonorrheal infection, vaginitis, et cetera).

Congenital.—This variety is analogous to, and frequently accompanies, congenital stricture in the urethra proper (three cases), at the bladder neck (one case), in the ureteral (two cases), intestinal and biliary tracts. An abnormally tight local embryonal closure of the urethral gutter occurs and in the absence of infection there is little or no sclerosis. Whether of embryonal correlation, when a long prepuce exists, a tight phimosis commonly accompanies a normally situated stenosed meatus. Parenthetically, at circumcision, if there is any question as to the adequacy of the meatal caliber, I routinely perform liberal meatotomy. In my experience, urethral stenosis common occurs in hypospadias (twelve cases in this series) and is the urgent consideration; it also occurred in one case of epispadias and in three cases of congenital torsion of the penis.

Acquired.—Urethral stenosis presenting the picture of sclerotic stricture may result from trauma or infection or the combination of these processes. This lesion is observed chiefly in adults, and particularly since the advent of transurethral prostatic resection and the more widespread employment of the indwelling catheter. Here localized meatal ulceration, due to the trauma, foreign body reaction and the constant moisture of the discharge which the catheter engenders, heals by sclerosis and produces stricture. Doubtless the incidence of meatal stenosis caused by instrumental trauma (sounds, cystoscopes, et cetera) is relatively small. In the male, urethritis may conceivably be an etiologic factor in some instances but as a rule the tight meatus passes unrecognized until the acquisition of gonorrhea or instrumentation directs attention to the condition. In three of our cases there had been "recurrent non-specific urethritis" and we believe this to be due to the tight meatus. In three boys, acute gonorrhea caused the pin-point orifice to be discovered; the youngest was three and one-half years old. In the female a persist-

ent or severe vaginitis may explain some instances of meatal stenosis and here the urethral lesion is definitely a sclerotic one. Yet we have observed the condition congenitally in several young girls in some of whom the excessive backpressure injury cystographically and cystoscopically presented the picture of bladder damage so commonly seen in advanced prostatic obstruction.

PATHOLOGY

Pathologically, the backpressure changes are usually greatest in the bladder, and, secondly, in the upper urinary tract; the complicating infection which may always be anticipated—for example, so-called "chronic pyelitis" in the young—accelerates the destructive process. Urinary infection was recorded in a fourth of our patients, in sixteen of whom the urologic examination was performed because of "chronic pyelitis."

In some instances the dilatation is localized to the lowest tract and particularly the urethra as was observed in a seven-year-old boy† admitted to the hospital because of hematuria. The bleeding was found to originate in a congenitally stenosed ulcerated meatus. The entire urethra and particularly the prostatic segment were markedly dilated; the bladder wall showed only slight damage and the uterovesical valve mechanism was still intact. Yet the extreme bulbous dilatation of the prostatic urethra was most unusual. In a newborn colored child an extremely large and apparently swollen prepuce was noted. A week later the obstetrical intern performed circumcision but at once found himself in a large ventral cavity connected with the urethral lumen. The operation was continued with removal of considerable tissue but not nearly all the urethral diverticulum which he failed to recognize. I saw the child the next day for the first time and found an exceedingly small urethral meatus behind which the diverticulum had formed as a blow-out process. Liberal meatotomy was performed and the channel distal to the diverticulum sac (measured 2 by 2 cm.) was kept widely dilated with sounds; six months later, drainage of the bladder by catheter inserted through a perineal boutonniere was followed by excision of the sac and closure of the urethra with a most satisfactory result. Yet the child is seen periodically for prophylactic urethral dilatation. A large urethral diverticulum at the base of

†Illustrated as figure 64 in Campbell, Meredith F.: Pediatric Urology. New York: Macmillan Co., 1937, Vol. I, p. 147.

the penis is a four-month-old child with persistent pyuria likewise formed as a blow-out behind a pin-point meatus (Fig. 1).

In a seven-year-old boy examined because of dysuria a tight external urethral meatus was found; cystoscopy and cystography

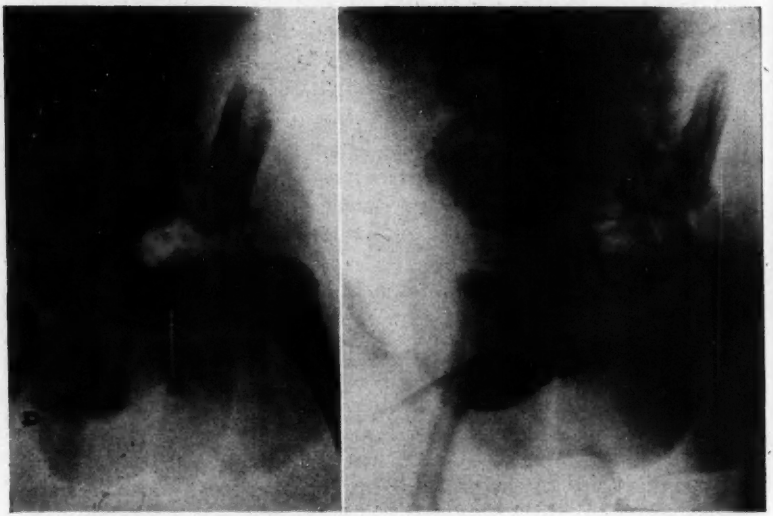

Fig. 1. *A (left),* Congenital stenosis of external meatus in six-month-old boy. Cystograms shows irregularity of bladder wall with bilateral vesico-ureteral reflux, more marked on left. Meatotomy; periodic dilatation with sounds. *B (right),* Cystogram one year later. Vesico-ureteral reflux is no longer evident on right but still persists on left. A vesical residuum of 4 ounces originally noted had now disappeared.

revealed widespread vesical sacculation with moderate dilatation.‡ No vesico-ureteral reflex was noted. Wide meatotomy and periodic progressive meatal dilatation to No. 22 F. was the treatment and was faithfully attended by the patient. Two years later irregularity of the vesical outline still existed but to far less degree than originally noted. Two girls, aged thirteen and thirty months respectively, were examined because of so-called chronic pyelitis. Each was found to have a tight congenital stenosis of the external urethral meatus with advanced trabeculation and sacculation of the bladder wall. The cystoscopic and cystographic pictures were those com-

‡Idem Figure 65, p. 148.

monly observed in advanced prostatic obstruction. Yet simple periodic dilatation with sounds, together with the administration of urinary antiseptics were curative.

Ureterectasis and hydronephrosis develop according to the se-

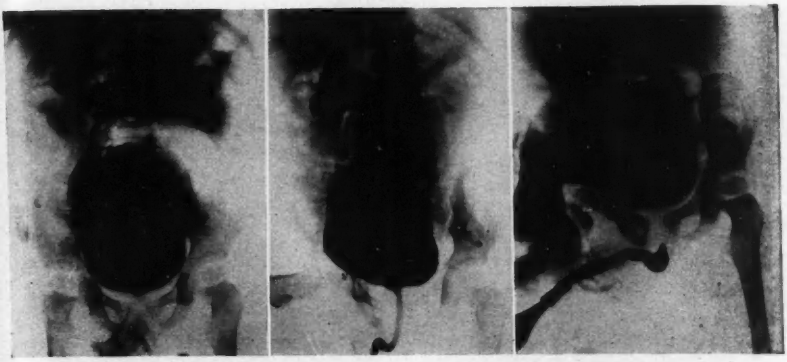

Fig. 2. Congenital stenosis of external meatus in eighteen-month-old male with balanitic hypospadias. The bladder was chronically overdistended with 500 c.c. of urine. *A* (*left*), Excretory urogram showing marked dilatation of upper urinary tract, particularly left hydronephrosis and great distention of bladder. Indwelling catheter employed for two weeks. *B* (*center*), Cystogram showing right vesico-ureteral reflux 1 month after *A*. It is notable that vesico-ureteral reflux is not present on the left. C (*right*), Urethrogram shows less urethral dilatation than one might expect to find with obstruction of such severity.

verity and duration of the obstruction. Extreme dilatation of the entire urinary tract above a stenosed urethral meatus was observed in a newborn child at autopsy at Bellevue Hospital; was seen clinically at thirteen days, and a few similar instances are reported in medical literature. Mild upper tract dilatation was cystographically demonstrated in a three-year-old girl with a stenosed urethral meatus. In an eighteen-month-old boy with a tight balanitic meatus, the entire upper tract was excessively dilated (Fig. 2); the residuum was 500 c.c. A No. 5 F. catheter was employed indwelling for one week; the meatus was incised and a No. 10 F. catheter was worn for another week. Thereafter the urethra was kept dilated (meatus No. 20 F.) and the urinary infection (Streptococcus hemolyticus, Staphylococcus aureus and colon bacillus) was eradicated with sulfadiazine. Six months later the anatomic restitution was only slight.

Yet the boy now empties his bladder and improvement in renal function attests successful therapy. A six-month-old boy presented the same picture with wide dilatation of the bladder and bilateral vesicoureteral reflux (Fig. 3). Here, also, striking functional improve-

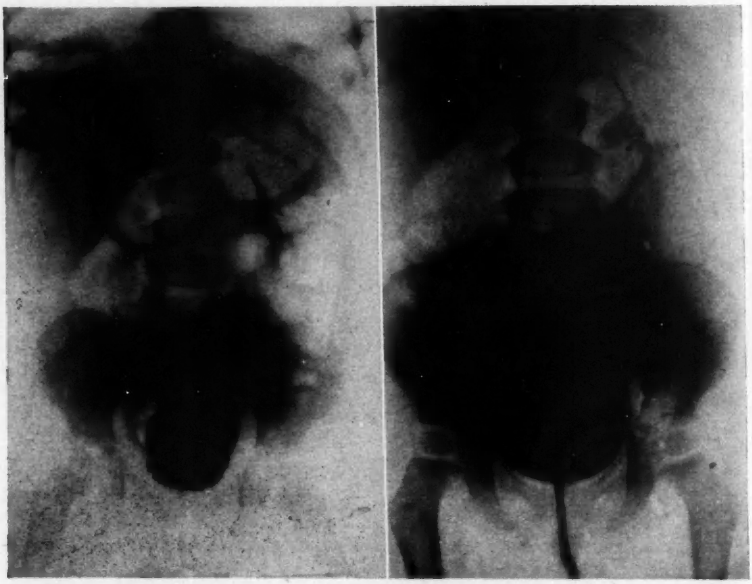

Fig. 3. Congenital stenosis of external meatus in four-month-old boy examined because of persistent pyuria and a large swelling at base of penis. The swelling proved due to a urethral diverticulum which had formed as a blow-out process behind the tight urethral meatus. *A* (*left*), Urethrographic demonstration of diverticulum *D* in antero-posterior urogram. B (*right*), Lateral urethrogram showing diverticulum outlined by ureteral catheter coiled in the sac and then passing to deep urethra. Meatotomy and periodic progressive dilatation with sounds were followed by striking diminution in size of diverticulum.

ment followed wide meatotomy and periodic progressive dilatation with sounds; considerable anatomic restoration was also observed. Vesical diverticulum was not observed in the children of this series who were cystoscopically studied, yet in two cases each there were vesical calculi, ureteral calculi and reduplicated ureters. In our failure to perform complete cystoscopic and urographic investigation in all these cases, it is probable that coexisting and/or com-

plicating urologic lesions were overlooked. Inflammatory and congestive lesions in the deep urethra, prostate, anterior trigone and especially the verumontanum are common with meatal stenosis. In five cases the enormously enlarged and engorged verumontanum extended well back into the vesical outlet.

Ulceration of the meatus is later discussed under Complications.

SYMPTOMS

Dysuria, frequency of urination and hematuria are the chief symptoms; 49 of these patients were examined because of so-called persistent enuresis and 16 because of "chronic pyelitis." Not only is there hesitancy in starting the stream, but the stream itself is unusually small and the pressure generated to force the urine through the tight meatus will sometimes throw this fine stream 6 to 8 feet. This is often accompanied by crying, screaming, strangury and a face red or purple from straining. As urine retained in the urethra leaks out slowly after urination there is terminal dribbling and wetting of the clothes. Chronic or recurrent vesical retention may be accompanied by leakage or overflow incontinence and in nine of our patients the obstruction produced abdominal pain. In short, the symptoms are those common to all lower urinary tract obstructions including the systematic manifestations of complicating infection and diminished renal function. With ulceration of the meatus, and with or without scab formation or incrustation, urination is apt to be especially painful and reflexly or consciously causes the patient to refrain from voiding. Yet as Brenneman has indicated, the application of cocaine to the tender meatus will temporarily permit painless urination. With meatal ulceration or the cracking of the scab covering the ulcer, the appearance of blood in the urine or on the child's clothing is most alarming to the parent who usually seeks medical attention for the child at once.

DIAGNOSIS

Diagnosis is by inspection and is utterly simple; should diagnostic confirmation be needed, employ exploration of the stenosed meatus with a surgical probe or small steel sound. When ulceration or incrustation of the meatus exist, their very presence should at once suggest the diagnosis.

TREATMENT

In males, my preference is liberal meatotomy with a fine scissors or

small scalpel at the outset and subsequent periodic progressive dilatation of the stenosed meatus with steel sounds. In children under one year of age it is our practice to keep the meatus dilated to at least No. 16 F. and in children from two to five years of age the dilatation is maintained up to No. 22 F. In females, instrumental dilatation is preferable to meatotomy. In this series meatotomy alone was performed in four cases (three acute gonorrhea), dilatation only was employed in thirty-one (including twenty-six females), and in the remaining 117 combined meatotomy and dilatation was the treatment.

At the time of the initial instrumentation, a small sound or bougie should be passed to the bladder to ascertain that there are no other congenital urethral obstructions. When possible, determination of the residual urine is of added value and is usually carried out at the time of the initial visit and meatotomy. In males we perform meatotomy and instrumentation without anesthesia and usually in the office. Mucocutaneous suture of the meatus is not required. Yet it is important that the mother or nurse be instructed daily to separate widely with her fingers the incised meatal margins. Despite this, there is usually fairly rapid closure of the opening and five to seven days after meatotomy we again dilate the meatus, at which time the healing wound will be re-opened. Occasionally it is necessary to do a secondary meatotomy. The meatal dilatation is repeated four or five times at lengthening intervals, and I prefer to see the patient again four to six months after he has been thought cured to ascertain that the meatus is still adequately open.

Co-existing infection is treated by the administration of urinary antiseptics and failure to achieve prompt sterilization of the urine, as indicated by two sterile cultures, calls for a complete urologic investigation; other congenital obstructions and/or lesions not recognized at the initial examination may be present.

COMPLICATIONS

The various complications of stenosis of the external meatus have been considered in previous paragraphs. Of these, ulceration of the meatus merits special consideration since apparently it is mysterious and perplexing to most physicians. The ulceration appears about the periphery of the stenosed meatus and usually extends 2 or 3 mm. within the opening. Although I have seen it in

the uncircumcised (three cases in this series), it is more common in boys who have been circumcised or whose short prepuce leaves the meatus well exposed. With drying of the ulcer, a scab or incrustation forms which further diminishes the meatal caliber or may completely seal it over between voidings. With cracking of the ulcer or scab, or pulling off of the incrustation by the clothing, active bleeding occurs; the blood may be in the urine or appear only on the diaper or underclothing. In the past this condition has been attributed to ammoniacal diaper, dietary indiscretion, too much cream and a host of other extraneous causes. Moreover, pediatrists who have been particularly interested in this problem, and notably Brenneman[2] and Cooke,[4] believe that the tight meatus is the result of the ulceration and not, as we believe, the basic cause of the erosion. In short, the stricture pre-exists—usually congenitally; ulceration follows, and the cycle of healing and further ulceration with progressive narrowing of the orifice ensues. The application of an array of salves and ointments, powders, the sterilization of the ammoniacal diapers, and other therapies have been widely advocated, chiefly by pediatrists, but I have yet to see a case not promptly and permanently cured by the establishment and maintenance of a wide urethral meatus.

SUMMARY

Urologic study of patients, and especially the young, with stenosis of the external meatus forcibly demonstrates the potential gravity of the obstructive lesion. In mild cases dysuria may be the only symptom; secondary ulceration of the meatus is likely to alarm the parent. Yet when eradication of the obstruction is neglected, back-pressure damage of the upper urinary tract is almost certain to ensue and even death from renal failure ultimately may occur.

The diagnosis is readily made by inspection and meatotomy is the treatment. Following meatotomy it is mandatory that the orifice be kept widely patent by periodic progressive dilatation with sounds until such time as the caliber of the meatus remains generously large.

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THE INTRAPROSTATIC INJECTION OF PITRESSIN AND ADRENALIN IN THE CONTROL OF BLEEDING DURING TRANSURETHRAL RESECTION

A PRELIMINARY REPORT

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Nearly everyone who has discussed transurethral resection of the prostate has commented upon the importance of bleeding during operation. When it is unduly brisk, it interferes with visualization of the field, and so prolongs the procedure. Moreover, a thin film of clotted blood may form upon the cut surfaces and lead the unwary surgeon to believe that a ragged, irregular surface is smooth, so that he stops the operation while there is still much to be done. This may result in continuing urinary retention, or in incomplete healing with late bleeding.

That excessive loss of blood may cause surgical shock and death is too well known to require comment here. The loss of a considerable quantity of blood may, without causing frank shock, so deplete the patient's resistance as to render him an easy victim of infection, and may undoubtedly interfere with healing of the wound. Hemorrhage may sometimes be followed by anuria and death without any evidence of surgical shock.

The deleterious effects of hemorrhage in the prostate are aggravated by the fact that the patient is usually an old man, and is too often debilitated by the secondary effects of his prostatism, and by other diseases attendant upon a long life.

The seriousness of the problem is indicated by the figures of Pilcher and Sheard, who measured the loss of blood during 110 operations with the knife punch and found that it averaged 384 c.c. The average amount of tissue removed per patient was 13.2 gm., a loss of 29 c.c. per gram of tissue.

Similarly, Nesbit and Conger, in a series of 100 consecutive transurethral resections, found that the bleeding averaged 169 c.c. per patient, with extremes of 4 and 1250 c.c. Since the amount of tissue removed averaged 20.37 gm., the loss per gram was 8.34 c.c.

Leaving aside individual experience and skill, there appear to be several factors which determine the amount of blood lost. First is the size of the gland: the larger glands have greater numbers of blood vessels (and hence more potential bleeding points), and the still unremoved but partially detached gland, being larger, can conceal more bleeders during operation than can the corresponding parts of the smaller glands. The fact that operation on the larger glands requires more time also increases the loss of blood.

A second factor of importance is the level of the blood pressure. If it be high, the greater driving force behind the blood tends to minimize spontaneous cessation of arterial hemorrhage, and to produce bleeding from more points. Moreover, the individual bleeder is more difficult to arrest by electrocoagulation because of the greater force behind it. The increased time spent in controlling bleeding thus materially increases the loss of blood.

The most reliable method of hemostasis is electrocoagulation of the bleeding point itself. Traction with the Foley bag is also valuable, but chiefly for venous bleeding, and is not satisfactory during the operation because its use involves so much loss of time.

Agents injected parenterally to increase the coagulability of the blood have, in my hands, been without value. These include hypertonic saline (Sexton), Koagmin, vitamin K, calcium salts, and Fibrogen. The author has had no experience with congo red (Hubly). Agents which reduce the blood pressure, such as amyl nitrite and nitroglycerine, ordinarily have such fleeting effects as to be useless, and, if effective, may promote the development of surgical shock.

In 1936, J. F. Emmett advocated the injection of 3 c.c. of surgical pituitrin directly into the prostate before or during operation to constrict the vessels and thus prevent bleeding, and reported his results in thirty cases. However, this dosage caused a rather severe systemic reaction, characterized by blanching of the skin, expulsion of large amounts of flatus, a sharp but transient rise in blood pressure, and, in all probability, a dangerous degree of constriction of the coronary arteries. In addition, the local vasoconstriction was so extreme and prolonged that there was real danger of bleeding after the conclusion of the operation. Emmett therefore abandoned the procedure. The writer used pituitrin in doses of 1 c.c. in a small series of cases shortly after Emmett's report, but desisted

when two patients in one day required postoperative hemostasis while, a short time later, coronary thrombosis developed on the cystoscopic table in a third patient who died in twelve hours in circumstances suggesting that the pituitrin was at fault.

Prolonged reflection made it seem that smaller quantities of this preparation or of pitressin might have desirable without harmful effects. Accordingly, during the past few months the writer has experimented with varying doses and dilutions of pitressin injected into or about the prostate just before or during the operation. Because adrenalin is a potent vasoconstrictor, yet is thought by some to dilate the coronary arteries, it has been added to the solution. The basic mixture thus far used consists of twenty to forty cubic centimeters of sterile normal saline containing three to four drops of pitressin and two to three drops of adrenalin. Neosynephrin, cobefrin, and ephedrine have been tried, but have seemed valueless.

Several routes of injection have been used. Most often a spinal puncture needle guided by a finger (which is protected by an O'Conor sheath) in the rectum is inserted into the periprostatic space, and 10 c.c. of the mixture is injected so as to surround the prostate as much as possible. This appears to be as effective as direct intraprostatic injection and does not distort the field. The solution may also be injected with a long McCarthy needle and an adaptor fitted with a telescope and inserted through the resectoscope. There appears to be but little to choose between the two methods, the former being more convenient before, and the latter after, introduction of the resectoscope.

In most cases following the injection, the surface of the gland is pale, and bleeding is at first strikingly diminished. There is often a sharp rise in the systolic pressure, averaging 20 mm. of mercury, and occurring within a few minutes, but ordinarily disappearing quite promptly. As a rule the blood pressure has, after the initial rise and fall, remained close to its original level; rarely has it been necessary to resort to any special measures to sustain or restore it, although spinal anesthesia has been used in most instances. In some hypertensive patients the blood pressure rises above its original level and remains there, and occasionally seems to aggravate the bleeding.

There is little or no blanching of the skin, and flatus is not

expelled. No patient thus far has had precordial pain or dyspnea, nor have there been subsequent coronary thromboses attributable to the drug. When, in from fifteen to thirty minutes, the vasoconstriction begins to wear off, no harm appears to result from the injection of more of the mixture (the McCarthy needle is most convenient here). The maximum volume of solution used so far has been 40 c.c., and the largest dose has been four drops of pitressin and two of adrenalin, but a trial of larger doses and of greater and lesser dilutions is contemplated.

The loss of blood during transurethral resection at the University Hospital has for some time been estimated by the method of Nesbit and Conger, so that it is possible to present actual measurements of the bleeding both in a control group and in patients given pitressin and adrenalin. It was intended originally to review a control series of 100 consecutive cases and a therapeutic series of about sixty, but it was found on studying the figures, that there was so little bleeding when less than 30 gm. of tissue was removed, either with or without a vasoconstrictor, that only those cases in which the specimen weighed more than thirty grams were included. Both series are consecutive and, in order to exclude personal variations, consist of cases operated upon by the author alone and within the past 18 months. No second-stage resections are included because bleeding is ordinarily much less profuse during a second operation.

There are fifty-one controls. The weight of the tissue removed averaged 57.9 gm. per patient, and the blood loss, 316.5 c.c. The largest single specimen weighed 133 gm., and involved the largest blood loss (1000 c.c.) in the series. Forty-five per cent lost more than 250 c.c. of blood. The average blood loss per gram was 5.45 c.c.

Thirty-two patients received pitressin and adrenalin. The tissue removed averaged 55.7 gm. in weight, and the blood loss 197 c.c. The maximum amount of tissue removed was 102 gm.; the maximum blood loss 550 c.c. (a 55 gm. gland in a hypertensive patient); 22.5 per cent lost more than 250 c.c. of blood* The blood loss per gram averaged 3.53 c.c., 1.92 c.c. per gram (35 per cent) less than in the control series (Pilcher reported twenty-nine and Nesbit 8.34 c.c. per gram in unselected cases).

Nesbit has pointed out that one must double the amount of blood

lost at operation to cover safely the probable postoperative loss. This was measured in these series only when it sufficed to occasion concern, so that figures relating to it are inadequate. In one case it was sufficient to necessitate evacuation of clots and electrocoagulation,

LOSS OF BLOOD AT OPERATION IN EIGHTY-TWO CASES IN WHICH 30 GRAMS OR MORE WERE REMOVED

SERIES	GRAMS REMOVED	BLOOD LOSS	BLOOD LOSS PER GRAM	PER CENT REDUCTION
Control	57.9	316	5.45	
Treated	55.7	197	3.53	35

In comparing the amount of blood lost in this and in the second series to that reported by others, one must remember that operations upon the small glands, and all second-stage operations, have been excluded by the author because of the small amount of hemorrhage which usually attends them, while other reported series include small as well as large glands.

but this resulted from failure to call the intern until a clot had blocked the catheter for more than an hour shortly after operation. In two other cases there was enough postoperative bleeding to prompt its measurement, but in no case did the combined operative and postoperative bleeding exceed 600 c.c. while eight of the control group lost this much or more at operation. Nevertheless, one must be scrupulous about stopping the bleeding before the patient leaves the operating room, and must be sure that the patient is kept there until the vasoconstriction wears off. The danger of postoperative bleeding is somewhat lessened by the tendency of the blood pressure, under the influence of pitressin and adrenalin, to remain at the pre-anesthetic level throughout operation.

SUMMARY AND CONCLUSIONS

The loss of blood constitutes one of the principal hazards of transurethral resection of the prostate. When excessive, it prolongs the operation, reduces its accuracy, and increases the risk of complications and of death.

The preliminary injection into the prostate of a mixture of normal saline, pitressin, and adrenalin is a series of thirty-two cases subjected to transurethral resection of 30 gm. or more has apparently reduced the blood loss by 35 per cent, and has been without harmful effects.

Care must be exercised lest the patient be returned to his room before the vasoconstricting effect of the drugs has worn off.

The series of cases is too small to permit the drawing of definite conclusions. More investigation is needed.

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DISCUSSION

DR. J. DELLINGER BARNEY: I would like to ask Dr. Keyes to tell us a little bit more about the point of issue of this ureter which he transplanted into the skin. Was it posterior?

DR. KEYES: It was where Hugh Cabot said to put it: put a cup between the ribs and the anterosuperior spine and bring the ureter out at the middle of the cup.

DR. BARNEY: And you had a cup for drainage?

DR. KEYES: Yes. Bobb makes the cup. It is named after one of my patients.

DR. BARNEY: That is what I thought; this being such an unusually successful case, you had some fancy way of doing it.

DR. KEYES: Oh, no.

DR. BARNEY: Do you know anything about the condition of the ureter at autopsy?

DR. KEYES: It was dilated, as you saw by the pictures. They are all dilated, they are all infected.

DR. BARNEY: Thank you!

Now, Dr. Campbell, I would like to ask if there is any preponderace of Jewish patients in these patients with stenosis of the urethra. Although I haven't any figures, I have an impression that the meatus in the Jew is more universally constricted, perhaps congenitally, than it is in the Gentile. I would like to ask Dr. Creevy, whose paper interested me immensely, if this solution of salt, pitressen and adrenalin, is of any value postoperatively. Supposing a day or two later or a week later hemorrhage begins, can this solution be used, and is it efficacious?

DR. LEON HERMAN: May I ask Dr. Keyes if he has any evidence in support of the belief that ureterostomy patients who wear an external appliance live longer on an average than those with indwelling catheters? One of our patients has been wearing catheters for seven years, another for nine years successfully; it is my im-

pression that the dangers of indwelling ureteral catheters have been much exaggerated.

DR. KEYES: I have operated upon only six cases. What do I know? My patients are more comfortable without a catheter in the ureter and I feel that without such a foreign body they are less susceptible to infection and secondary stone.

DR. HUGH H. YOUNG: Dr. Keyes' case of ureterostomy interests me greatly. Undoubtedly, permanent ureterostomy and also nephrostomy have a very important place in urology.

I have a case (BUI No. 13484) in which the patient came to me as a girl of sixteen with staghorn calculi in both kidneys. During the following sixteen years that intervened, I thought it necessary to operate first on one and then on the other kidney to remove calculi, and as they recurred again, I operated on each side. Finally, two years ago the patient came back to me with extensive recurrence of calculi in both kidneys and severe uremia. I first operated on the left side and removed as many calculi as I could, then inserted a rubber tube for permanent drainage. A few weeks later I carried out a similar procedure on the opposite side. She had a close call after these operations, but the rubber drains worked well, and in a short time she got over her nausea and vomiting, and her blood urea began to improve. Since then I have followed her over two years. She is still wearing the rubber drains. The bilateral nephrostomy has allowed her to regain excellent health. The blood urea is almost normal, and she has no pain, although each kidney contains numerous calculi. I simply brought out these tubes through the anterior part of the lumbar incision. They pass through an elastic girdle and down into a rubber urinal. The girdle holds them in place, and the patient has no discomfort and is enjoying excellent health.

DR. HERMAN: I think some warning should be voiced about doing bladder operations with trophic disturbances as the result of cord lesions. An illustrative case is that of a girl with complete urinary incontinence, who had been operated on in early childhood for sacral meningocele. At the age of fourteen she was admitted to the Pennsylvania Hospital where I tried to do a fancy operation which entailed closing the internal urinary meatus and making a type of cystotomy that would enable her to catheterize herself through a

trap-door affair. The wounds broke down. Subsequently we mobilized the urethra, inverted and ligated it, and sewed the vaginal wall over the site; this, too, broke down. The patient had partial incontinence of feces, which seemed to preclude successful ureteral transplantation into the bowel. However, we next transplanted fascia lata by the Stone method as a means of strengthening the tone of the rectal sphincters and thought we had succeeded, since she was able to retain enemas satisfactorily. We then transplanted the right ureter into the sigmoid, but, unfortunately, the sphincter muscles could not retain the urine and feces. Bilateral ureterostomy was then done, and the patient is now dry and quite comfortable. Incidentally, the girl has since been married. I might add that a satisfactory way of collecting the urine with a tube in the ureter is by means of an ordinary surgical glove, tied to the tube by means of a tape which latter may be pinned to the clothing. By providing the patient with a dozen gloves or more, the odor that invariably attends the use of ordinary urinals can be eliminated. A new glove is applied each time it is necessary to empty one so that each glove is not used more than once every three or four days and can be kept sweet and clean.

Our patients, especially the ladies, much prefer this method to any type of urinal that we have been able to provide.

DR. GEORGE R. LIVERMORE: May I say a word about prostatic resection? I think Dr. Creevy is to be complimented upon the work he has done, but it has been my experience that if we will stop all hemorrhage before the patient leaves the operating room and free drainage is maintained, we do not have much trouble afterwards.

The injections of material into the prostate and around the prostate are not devoid of danger. I believe that the less manipulation we do, the better these patients progress. I make it a rule, when I have a severe case of hemorrhage and have great difficulty in controlling it, to stop the operation, put in a Foley bag catheter, exert traction, and send the patient back to his room. The increased drainage reduces congestion and the size of the prostate. Therefore, when the second operation is done, the bleeding is greatly reduced. It is a good rule to control the hemorrhage after each cut, as it is difficult to see where to fulgerize when blood is spurting from several areas.

DR. KEYES (for Dr. Quinby): He was going to say, then you are going to operate on them all over again. I said "Sure, that is the advantage."

DR. LIVERMORE: Yes, operate on him a second time and save his life rather than complete the first operation and have him bleed to death. That is my principle, to discontinue the operation when the hemorrhage is severe and difficult to control and let the congestion subside. Then complete the operation later. It is much better to have a live patient with a prostate than to have a dead one without one.

In regard to Dr. Campbell, I think he is to be congratulated for bringing this subject out. In teaching my students, I have always emphasized the fact that a small meatus is responsible for back-pressure with bladder and upper urinary tract damage. If we could emphasize this more to the general practitioner and the obstetrician, it would be far better than bringing it before a class of gentlemen like you who have heard it.

DR. HUGH H. YOUNG: Just to add an inflammatory note to this discussion, may I suggest to these gentlemen, who are going to such great trouble to determine how much blood the patient loses after transurethral resection and how much the patient can stand without dying, that they would do well to take up perineal prostatectomy in these larger cases of prostatic hypertrophy. You can thereby see what you are doing, detect the bleeding vessels, clamp and tie them, and then close the wound so that the mucous membrane of the vesical neck and urethra completely covers the defect left by the enucleation of the prostatic lobes. By so doing, hemorrhage is completely controlled and per priman healing is usually obtained. You won't have to wait several weeks for the cauterized tissues to loosen and pass out and for epidermization to cover the defect, and chronic prostatitis will not continue to vex you and the patient. For full details, see an article of mine in the July 1943 issue of *Surgery, Gynecology and Obstetrics.*

DR. MEREDITH F. CAMPBELL: In answer to Dr. Barney's question regarding an abnormally high incidence of ulcerated meatus among Jewish children, in New York two-sevenths of the population are Jews and this has been approximately the incidence as I have observed it. As to circumcision, you find practically all the

children in better economic surroundings have been circumcised as a sort of obstetrical encore, so the glans penis is exposed and if ulceration occurs, there is likely to be incrustation.

DR. C. D. CREEVY: I find that I forgot one of my preliminary remarks. I had intended, in presenting the suggestion that pitressin be used in transurethral resection, to say that I did not wish to reopen any old wounds in connection with the choice of operation on the prostate.

In reply to Dr. Barney's question, it has occurred to me to use pitressin postoperatively, but the occasion on which it might be satisfactory has not yet arisen. There is one other thing I neglected to mention and that is there have been no deaths in this series of thirty-two cases. Well, of course, that doesn't mean anything. The group is much too small. But some thirty or forty cases in which less than 30 grams were excised were done without fatality during this period. I should have mentioned, too, that in order to make the thing uniform, I have omitted all cases in which anyone else had a hand. These were all done by me and there were no second-stage resections included because of the smaller blood loss there which would throw off the figures.

DR. BARRINGER: May I ask just one question? You say you wait a half hour until after the pitressin has lost its effect. Suppose the patient bleeds after that, what do you do?

DR. CREEVY: So far only one patient has done so. He was returned to the operating room for electrocoagulation of the bleeders. I think that is far better than to fuss around while the patient loses a lot of blood.

THIRD DAY, JUNE 12, 1943

EXPERIENCES WITH THE DEMING NEPHROPEXY

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Nephroptosis has occupied a prominent place in urological literature since 1841 when Rayer described the movable kidney as a definite clinical entity with characteristic signs and symptoms. In 1881, Hahn performed the first nephropexy, resecting a portion of the fatty capsule and suturing the perirenal fat to the lumbar incision. Because of recurrences resulting from the rather loose attachment made by suturing the fatty capsule to the lumbar wound, Bassini modified Hahn's operation by taking sutures through the fibrous capsule of the kidney. Since Hahn's original operation was described, numerous methods of suturing the kidney in place have been devised; in fact papers on this subject usually present a new operation or some modification of an old operation. At the present time most surgeons who perform nephropexies fix the kidney by sutures through the intact or reflected capsule by strips of fascia reflected from the renal capsule or nearby structures, or by suturing the perirenal fat and fascia to the lumbar muscles below the kidney.

Any of these operations may be successful if the kidney is properly prepared and care is taken to suture it in its normal anatomical position. Operations upon the kidney are always followed by rather extensive adhesions. Actual recurrence of renal ptosis is rarely encountered. The poor results that follow nephropexy are usually from the improper selection of cases, from faulty technique in which some accessory pathologic condition is not corrected, or the kidney and ureter are not completely liberated.

An important part of the operation is complete liberation of the upper ureter and pelvis and careful dissection of all perirenal fat and fascia from the kidney. The ptosed kidney is often complicated by adhesions to the ureter, by aberrant vessels or by ureteropelvic pathologic lesion. When there are no such complications, pro-

nounced degrees of renal mobility are often found in which the kidney empties normally with no discomfort to the patient.

Regardless of the method of suspension to be used, the preparation of the kidney and its bed is the same. Adequate exposure is necessary so that the kidney, the upper portion of the ureter, and the renal fossa can be easily seen. An ample curved lumbar incision is usually most satisfactory, though it is rarely necessary to divide the posterior fibers of the oblique muscles of the abdomen. After making the incision and ligating all bleeding vessels, the operation is continued by first separating the posterior portion of the perirenal fascia from the lumbar muscles as far posteriorly as practical. A longitudinal incision is then made in the fascia about opposite the medial border of the kidney and is extended both upward and downward.* A clean incision in the fascia permits it to be reflected forward and preserved for use in protecting and supporting the kidney when it has been placed in its bed.

The fascia after having been divided is carefully dissected from the kidney and, together with the perirenal fat, is reflected medially, carrying before it the parietal peritoneum. These structures are retracted anteriorly, giving adequate exposure to the kidney and renal fossa. When adhesions from the perirenal fascia to the kidney are not readily separated by blunt dissection, they should be divided with scissors to prevent tearing the renal capsule. The kidney thus exposed is held by an assistant while the surgeon separates all adhesions from the lower pole of the kidney, beginning at the convex border and continuing around the lower pole until the ureteropelvic area is reached. Small blood vessels entering the lower pole are ligated and divided, but if a vessel is large enough to supply an extensive area of the kidney, it should be preserved.

When the ureteropelvic area is reached, the ureter is identified and carefully liberated as far downward as can be done with safety. All adhesions are divided and any kinks or other obstructive lesions are corrected. Adhesions are then separated from the renal pelvis and the ureteropelvic area is examined. If there is stenosis of the pelvic orifice or high implantation of the ureter, an appropriate plastic operation should be done. After the lower pole, pelvis and ureter have been freed of adhesions, the assistant retracts the kidney downward, slightly elevating the upper pole while all fat and adhesions are separated from this area and from the vascular ped-

icle. The kidney is now ready to be fixed in place. The renal fossa is prepared by removing all fat and fascia from the lumbar muscles well above the costal margin. Occasionally, the liver encroaches upon this area and light adhesions must be broken up to permit the kidney to be placed in a sufficiently elevated position.

Until recently I have combined the principles of the operations devised by Howard A. Kelly and Clyde L. Deming. Two suspending sutures are used. The first suture is placed at about the junction of the middle and lower thirds of the kidney and the second suture near the lower pole. These sutures are carried through the margin of the quadratus muscle, the first suture as high up as it can be conveniently placed and the second an appropriate distance below the first. After the kidney has been elevated in position and the sutures are pulled taut, the kidney elevator of the table is lowered and the kidney and ureter are again examined before the sutures are tied. To insure good drainage of the lower calyces the upper pole of the kidney should point a little medially and the lower pole outward. The ureter should be straight but not taut and there should be no tension on the vessels of the renal pedicle.

If all is in good order, the suspending sutures are tied. The perirenal fascia and fat are then brought across the anterior surface of the kidney and sutured to the lumbar muscles immediately below the kidney. Two sutures are used, one about a centimeter external to the ureter and piercing the fascia near the edge of the peritoneum, and the other piercing the muscle and fascia about five centimeters lateral to the first suture. These sutures are placed beneath the lower pole of the kidney and when they are tied the space beneath the kidney is partly obliterated and the fascia forms a sling beneath the lower pole which gives additional support. A rubber tissue drain is then inserted behind the kidney and the wound is closed.

For the past three years I have discontinued the use of the suspending sutures and depend entirely upon the perirenal fascia and fat to hold the kidney in position. No sutures are placed in the kidney or its capsule. The following paragraph is from Deming's description of the operation:

"The perirenal fat is all stripped off the kidney which, with its vessels and ureter, is then delivered into the wound. It is important that all adhesions be removed from the upper as well as the lower pole. The ureter, which is either tortuous or badly kinked, should

be made free. Special attention should be noted concerning the kidney fossa—whether shallow, absent or deep. The liver sometimes is adherent to the posterior abdominal wall so that it is impossible to place the kidney in its bed without freeing the right lobe. The

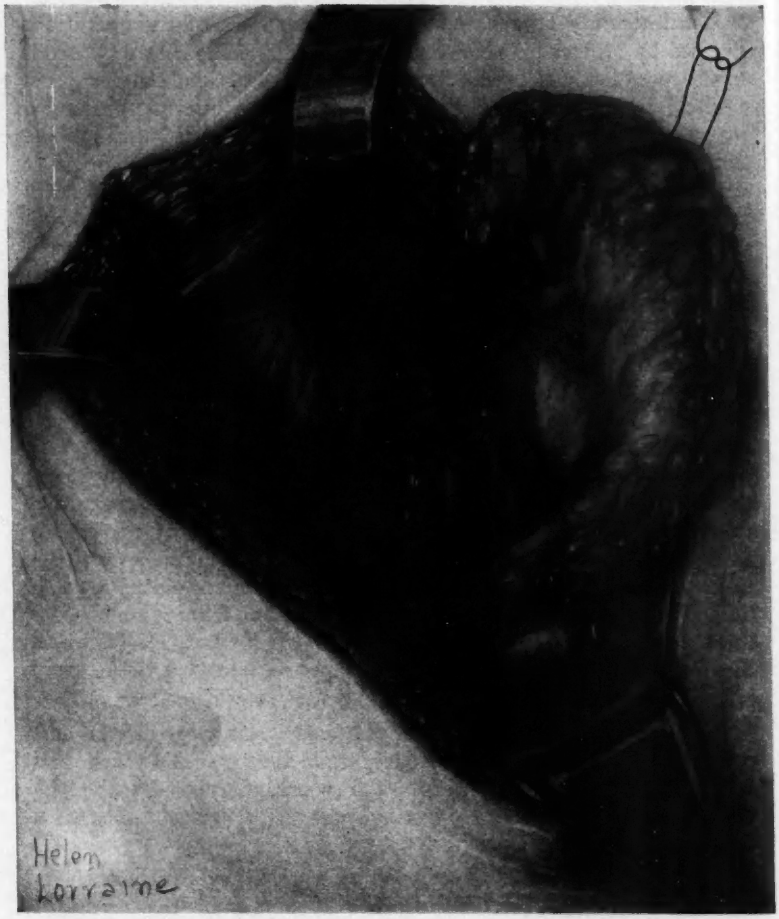

Fig. 1. With the kidney held in position the first interrupted mattress suture is placed through the perirenal fascia and peritoneum to the quadratus muscle about one centimeter from the ureter.

hand should be inserted under the right lobe of the liver to the diaphragm. When this is done, the kidney can be replaced sufficiently high to remove all kinks and most of the tortuosities of the ureter. The kidney can be made to occupy practically an intratho-

Fig. 2. The sutures have been placed and tied forming a sling of the fat and fascia which holds the kidney in a normal position. The wound is usually closed without drainage.

racic position with the lower pole lying opposite the last rib. The upper pole should be carried medially and the lower pole outward to give independent drainage to the lower calyx. With the kidney

held in position a series of interrupted mattress sutures of No. 0 chromic catgut is placed through the perirenal fascia and peritoneum to the quadratus muscle. Perirenal fascia is always excessive so that it is easily approximated. Precautions must be taken not to include the bowel medially. The first stitch should be placed about 1 cm. from the ureter and as high as possible on the quadratus muscle posteriorly (Fig. 1). Care should always be taken not to include any nerves in these sutures of chromic gut. A series of five to eight sutures is necessary to close this aperture. These form a basket sling for the kidney so that it is impossible for the organ to descend (Fig. 2). This row of sutures is now reinforced by bringing up all the extraperitoneal fat and suturing it with two or three mattress sutures to the quadratus muscle below the other line of sutures. This fat acts as a support and fills the space previously occupied by the kidney. The wound is then closed in layers with No. 2 plain catgut and the skin with interrupted silk without drainage."

Deming's operation is certainly the most physiological of any so far devised. Neither the kidney nor its capsule is disturbed, and it is held in place at least in part by normal support. Adhesions certainly occur between the renal capsule and the kidney bed to help hold the kidney in place. In my experience removal of a portion of the capsule is not necessary for this purpose.

From January, 1940, until January, 1941, eighteen patients were operated upon for the relief of renal ptosis. There were three males and fifteen females. Their ages ranged from thirteen to fifty-two years. The duration of symptoms varied from one to ten years; the average was four years. Eight patients complained of repeated attacks of pyelitis, two were examined because of frequency of urination and a history of pyuria. The remaining eight complained of pain in the loin and abdomen. Three of the eighteen patients had had gastro-intestinal studies because of indigestion. The ptosis was complicated by stone in two patients and a plastic operation on the renal pelvis was necessary in three.

Sixteen patients have been entirely relieved of their symptoms. Two, not entirely relieved, have general viceroptosis and have been treated for indigestion and abdominal pain for many years. They have both been relieved of the acute attacks of pain which before they were operated upon occasionally required opiates.

The following case reports are characteristic of this group of patients.

CASE REPORTS

Case 1.—Mrs. A. H. H., twenty-one years of age, was admitted to

Fig. 3. Case 1. Bilateral nephroptosis before operation.

St. Elizabeth's Hospital, January 11, 1940. She had suffered with frequency of urination for five years. At times she had had cloudy urine and burning on urination. About a month before her admission to the hospital, she had an acute attaek of pyelitis while visiting in Atlanta, and was examined by Dr. W. E. Upchurch, who found that she had bilateral renal ptosis (Fig. 3) and advised nephropexy because of the long history of urinary infection.

January 12, the right kidney was operated upon. The operation combined the principles of the Kelly and Deming operation described in this paper. Ten days later the left kidney was suspended by the Dem-

ing method. The bilateral pyelogram taken in the upright position three weeks following the second operation (Fig. 4) shows both kidneys in good position and definite improvement in the appearance of the calyces. Following this experience the fixation sutures as employed by Kelly

Fig. 4. Case 1. Intravenous pyelogram one month following bilateral nephropexy.

Fig. 5. Case 2. Right renal ptosis before operation.

were abandoned as time-consuming and unnecessary. This patient has been entirely relieved of her discomfort and pyuria and has gained 20 pounds.

Case 2.—M. O., female, aged forty-two years, was admitted to the Hospital Division of the Medical College of Virginia August, 1941, because of pain in the right lumbar area and right side of the abdomen. She had been previously admitted twice because of the same complaint. A diagnosis of right renal ptosis had been made and palliative treatment including a ptosis belt had been prescribed with very little benefit. She has been in almost constant pain for two years. The physical examination was negative except that she was underweight and the right kidney was palpable and tender. There was moderate pyuria. Retro-

grade pyelogram with the patient in an upright position showed decided right renal ptosis (Fig. 5). A nephropexy was done. She recovered rapidly and within ten days was comfortable. The pyelogram made one month following operation (Fig. 6) showed the kidney in good posi-

Fig. 6. Case 2. Postoperative retrograde pyelogram.

tion. This patient, a frequent visitor to the outpatient clinic before operation, has remained free of pain for the past two years.

Case 3.—I. R., a seventeen-year-old boy, was admitted to the Hospital Division of the Medical College of Virginia in July, 1942, because of pain in the right lumbar area and right upper quadrant of his abdomen. He had complained of indigestion and abdominal pain for more than a year. An x-ray examination of his intestinal tract a year before his admission to the hospital was negative. He stated that for several months when riding a horse he fastened a wide belt around his waist quite snugly to prevent pain in the right loin. An intravenous pyelogram was done because of pain in the right loin and pyuria. The left kidney appeared normal and the function of the right kidney was too poor to give a clear outline of the renal pelvis. A retrograde pyelogram

(Fig. 7) done the day following his admission to the hospital showed slight ptosis and evidence of ureteropelvic obstruction. Following this pyelogram he became quite ill with high fever, rapid pulse, and muscle spasm over the right lumbar area. An effort to pass a catheter into the renal pelvis was unsuccessful. Immediate renal drainage was consid-

Fig. 7. Case 3. Preoperative pyelogram. There is moderate ptosis and evidence of ureteropelvic obstruction.

Fig. 8. Case 3. Intravenous urogram three months following nephropexy and plastic operation on right ureteropelvic junction.

ered necessary. At operation the kidney was found greatly congested with a large pelvis distended with purulent urine. There was a definite kink at the ureteropelvic junction. After freeing the kidney of adhesions, the urine was aspirated from the renal pelvis through a large needle. A short longitudinal incision was made through the ureteropelvic area and a No. 10 urethral catheter was inserted down the ureter about 4 inches. The proximal end of the catheter was passed out through a stab wound in the posterior wall of the pelvis. A small window was cut in the portion of the catheter lying in the pelvis. The tip of a larger catheter was drawn into the pelvis through the renal parenchyma near the lower pole for additional drainage. The incision at the ureteropelvic junction was then closed transversely, increasing the width

of the pelvic orifice. A rubber tissue drain was placed behind the renal pelvis and a nephropexy was done. The patient's temperature which was above 105 F. at the time of operation did not go above 102 F. the following day and was normal within a week. An intravenous pyelogram done three months after the operation (Fig. 8) showed the kidney

Fig. 9. Case 4. Renal ptosis with kinking of ureter and dilated renal pelvis.

Fig. 10. Case 4. Postoperative intravenous urogram. Note improvement in contour of the renal pelvis.

in good position with good function and the urine was entirely normal. He returned to a military school in September, 1942, and has taken part in the regular activities without discomfort of any kind.

Case 4.—L. W., a thirteen-year-old girl, was admitted to the Medical Service of the Hospital Division of the Medical College of Virginia, September 18, 1942, because of fever and pain in the right lower quadrant of the abdomen. The urine contained numerous pus cells. The patient gave a history of four similar attacks during five years previous to her admission to the hospital. The acute symptoms re-

sponded to rest in bed and the administration of sulfathiazole. An intravenous pyelogram showed definite dilatation of the right renal pelvis and a tortuous ureter. On October 12, she was transferred to the urological service, and a retrograde pyelogram was made of the right kidney with the patient in the upright position. There was definite ptosis of the kidney, dilatation of the renal pelvis with a tortuous irregularly dilated ureter (Fig. 9). Two days later a nephropexy was done. The convalescence was uneventful and the pyelogram made three weeks later showed the kidney in good position with definite reduction in the size of the renal pelvis (Fig. 10). She was discharged entirely free of symptoms and has remained in excellent health.

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TWELVE-YEAR SURVIVAL WITH ONE-HALF OF ONE KIDNEY

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It is well known that the amount of renal parenchyma present in the normal adult is greatly in excess of the amount necessary to insure the prompt discharge of the renal responsibilities of normal life. It is likewise well known that life can be maintained after the major portion of the renal parenchyma has been rendered inactive by surgery or by disease such as polycystic disease, chronic nephritis, bilateral hydronephrosis or pyonephrosis. Undoubtedly there are many nephrectomized individuals who are successfully maintaining life although their remaining kidney is partially destroyed by disease.

Life of laboratory animals has been successfully maintained for long periods of time after the surgical removal of 75 per cent of their renal parenchyma, but we know of no recorded incident in the human being in which both a nephrectomy and a heminephrectomy have been successfully performed. For that reason we wish to report the case of a woman who has lived twelve years with one-half of one kidney. During this twelve-year period she has led a normal life and with the exception of a pregnancy, a cholecystectomy, and recently the menopausal cycle, has been perfectly well.

CASE REPORT

Mrs. M., aged thirty-eight, was admitted to Christ Hospital July 2, 1930, with a history of about a year's duration. The important points in the history were attacks of intense pain and discomfort in the region of the left kidney, marked dyspeptic symptoms, loss of weight, frequent chills, high temperature, and severe bladder symptoms. There were no symptoms suggestive of involvement of the right kidney.

On examination she was found to be underweight, quite anemic, with a large, easily palpable, painful mass in the region of the left kidney. The urine showed pyuria grade 4. The functional output was 35 per cent. Her blood urea was 30 mg. Blood pressure was 118/80. Roentgenological studies showed multiple large stones in the region of the kidney fossa on either side (Fig. 1). Retrograde studies of the

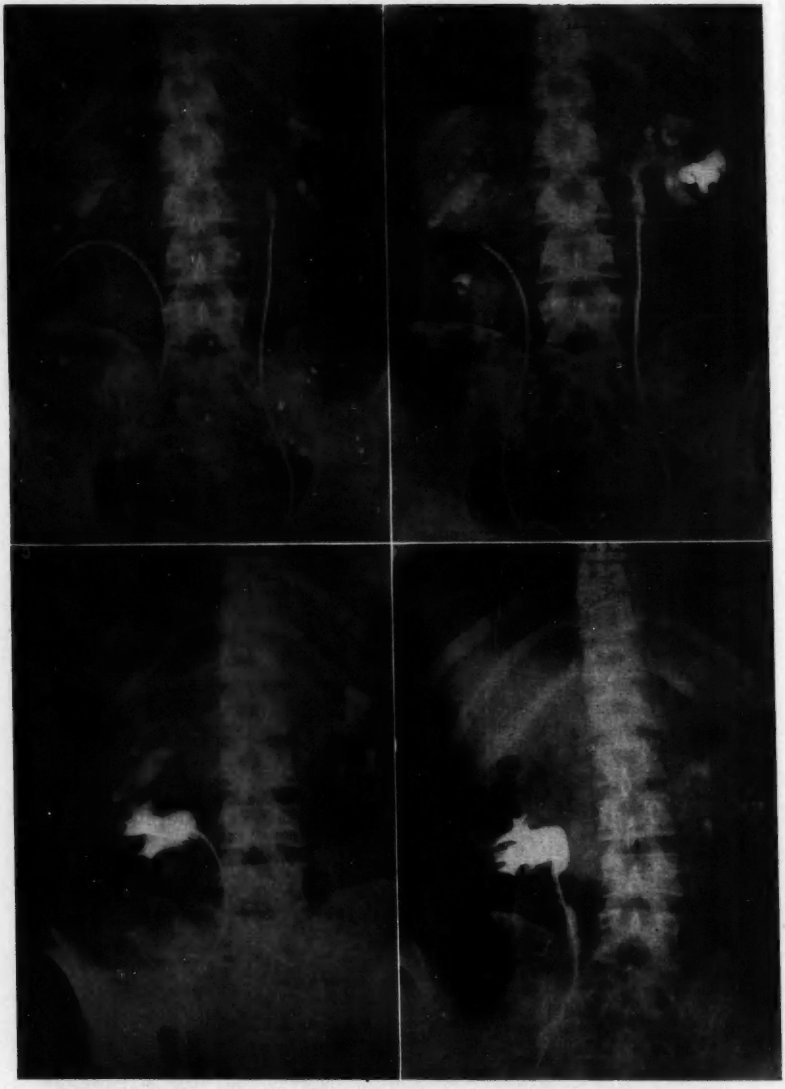

Fig. 1. (*Upper left*) Massive bilateral calculous pyelonephritis.
Fig. 2. (*Upper right*) Left pyelogram shows extensive damage to left kidney and an almost complete occlusion of upper portion of left ureter by a calculus. (A remnant of pyelographic medium is shown in lower calyx of right kidney.)
Fig. 3. (*Lower left*) Pyelogram of lower half of right kidney.
Fig. 4. (*Lower right*) Pyelogram made two months after resection of upper half of right kidney. There is a nephrotomy tube in the left kidney.

upper urinary tract showed massive calculous pyonephrosis on the left side with a stone impacted in the upper end of the left ureter (Fig. 2); on the right, massive calculous pyonephrosis of the upper half of the double kidney; moderate degree of extra renal hydronephrosis of the lower half which was uninfected and free of stones (Fig. 3).

Because of the patient's poor general physical condition several days were utilized in preoperative care. She was given several transfusions of both blood and glucose. On July 11, 1930, a left nephrolithotomy was done. Approximately 700 c.c. of very thick, heavy purulent material was drained from this large abscess of the left kidney and as many of the stones as could be reached were removed. A nephrotomy tube was left in position.

The patient made a perfectly magnificent recovery and on August 5, four weeks after draining the left kidney, a right heminephrectomy was done (Fig. 4). Recovery from this was uneventful. We believed that several months should elapse before the removal of the large pyonephrotic left kidney should be attempted.

On September 29, 1930, the patient was readmitted to the hospital for replacement of the nephrotomy tube. Functional test at this time was 40 per cent; her blood pressure 130/90; blood urea 28 mg. Urine was reported as showing a trace of albumin and occasional casts.

In February, 1931, she was readmitted to the hospital with a complaint of pain in her right side. Studies of the right kidney showed a very indefinite shadow in the region of the right renal pelvis (Fig. 5). Retrograde pyelograms showed a rather large area of lessened density which corresponded to this shadow (Fig. 6). On March 7, 1931, seven months after the heminephrectomy, a right pyelotomy was carried out without difficulty. We removed an organized blood clot about which there was a thin shell of urinary salts. Undoubtedly this was a sequela of the heminephrectomy seven months previously.

She made a perfectly magnificent recovery from this operation and on April 20, eight weeks after the right pyelolithotomy, her functional output was 45 per cent; her blood pressure 130/86; her blood urea 28 mg. On April 21, 1931, nine months after the original nephrotomy, a left nephrectomy was done. The less said about the technique of that operation the better; it is only necessary to say that it was a tough job and that the patient's condition did not allow the removal of the upper portion of the ureter containing the impacted stone.

On May 26, 1931, the patient was dismissed from the hospital in excellent condition with the exception of a draining sinus from her left side. This sinus continued to drain. Occasionally there would be the formation of a small abscess, but in spite of that the patient's general physical condition improved remarkably. On July 1, 1931, a right pyelogram was made. The sinus was injected with lipiodol to determine its course and, to be quite honest, in order to be sure that the stone was the only foreign body (Fig. 7).

On May 1, 1932, she was readmitted to the hospital for another at-

Fig. 5. (*Upper left*) Shadow of moderate density in region of right renal pelvis six months following heminephrectomy.

Fig. 6 (*Upper right*) Area of lessened density in pyelogram corresponding to shadow shown in Figure 5. Left nephrotomy tube has been temporarily removed.

Fig. 7. (*Lower left*) Lipiodol injection of persistent fistula following left nephrectomy.

Fig. 8. (*Lower right*) All calculi have been removed.

Fig. 9. Right pyelogram two years after heminephrectomy.

Fig. 10. Absence of calculi thirteen years after right heminephrectomy and twelve years after left nephrectomy.

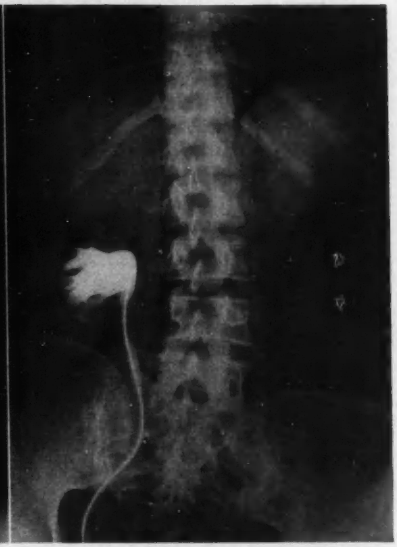

Fig. 11. Right pyelogram thirteen years after heminephrectomy. There has been no increase in amount of extra-renal hydronephrosis or change in the calyces.

tempt at the removal of this stone which was acting as a foreign body and was preventing the healing of the sinus. Her blood pressure was 134/94; blood urea 23.8 mg.; functional output 43 per cent. On May 3, twenty-two months after original left nephrotomy, we were successful in removing the stone. Patient remained in the hospital only about ten days; her side promptly healed (Fig. 8). She was free of all symptoms and plain x-ray was negative for shadows suggestive of urinary calculi. Her urine at this time contained 1 plus albumin.

On August 14, 1934, four years after original admission, the patient was again admitted to the hospital complaining of pain in her right side. On examination we found that her right kidney was perfectly normal (Fig. 9) but that she had a gall bladder full of stones. At this time her functional output was 55 per cent; her blood urea 36.8 mg.; her blood pressure 148/90. A cholecystectomy was done by Dr. Reed Shank. The patient's postoperative course uneventful.

About two months prior to this last admission to the hospital the patient gave birth to her seventh child. As she lived in a distant city we knew nothing of this situation until this time.

The patient was seen for routine examination on December 18, 1939, at which time the functional test was 32 per cent; blood pressure 150/92; blood urea 26 mg. She was complaining of some headaches and albumin was still 1 plus. She had definitely entered the menopausal cycle and was quite apprehensive and worried about herself. She was seen again in March, 1941, at which time her blood pressure had risen to 184/120. She was complaining of rather severe headaches; blood urea was 38 mg.; functional test 40 per cent.

Since that time she has been under the care of a very competent medical man. The symptoms of her menstrual cycle have been definitely reduced. Her blood pressure now is 160/100; she is practically free of her headaches.

Functional test on May 15, 1943, was 36 per cent and blood urea 28 mg. With the exception of this hypertension she is in excellent condition. Plain radiograph was negative for stone (Fig. 10). Retrograde pyelogram showed no increase in the extrarenal hydronephrosis and the calyces were well cupped (Fig. 11).

Throughout this presentation the functional test data are based on the following technique: 1 c.c. phthalein is injected in the gluteal region. Ten minutes is allowed as the time of appearance and two specimens of one hour each are then collected.

As well as the above figures we have frequently made fractional functional tests in which our collection periods following intramuscular injection have been twenty in number and of five minutes each. The per cent per cubic centimeter of each specimen has been determined. From these tests we see a gradual shift of the time of maximum concentration of the dye from a point shortly after injection to a point approximately one hour later. This, of course, is significant of alteration of the functional capacity of the kidney.

The patient does have hypertension which undoubtedly is at least in part due to the small amount of renal parenchyma she has. We believe it is also in part due to her menopausal manifestations. She has always had a fair amount of albumin and usually some granular casts, but at no time has she shown evidence of edema in any part of the body.

ADRENAL HETEROTOPIA, RESTS, AND THE SO-CALLED GRAWITZ TUMOR

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THE RENAL HYPERNEPHROMAS

There is no more confusing chapter in the whole of pathology than that which deals with the origin of the most frequent malignant tumor of the kidney in adult life—the so-called Grawitz tumor or hypernephroma.

The various arguments as to whether these tumors are of adrenal or renal origin depends on evidence based upon their cellular characteristics; upon various embryological theories; functional concepts; and chemical assay for the presence or absence of cortin or any masculinizing hormone.

Argument Based Upon Cellular Histology.—In 1883, Grawitz[1] proposed the well known theory that these tumors arise from misplaced bits of adrenal tissue.

This theory was based entirely upon the histological appearance of the tumor, namely, the large, clear, polyhedral cells with their pronounced tendency to store fat in their cytoplasm; the thin septa with thin-walled capillaries; and the general resemblance to adrenal cortical tissue. It was further supported by the well known fact that small nodules of what appeared to be cortical adrenal tissue were frequently observed beneath the capsule of the kidney and scattered along the courses of the descent of the genital glands and ascent of the kidney during the early life of the embryo.

In 1893, Sudeck,[2] and in 1908, Stoerk,[3] rejected the Grawitz theory, claiming also on purely histological grounds that these tumors were renal in origin and developed directly from the well known adenomas which originate from renal tubular epithelium and are so frequently found in the sclerotic kidney.

The arguments of these workers against the adrenal origin of the hypernephroma were based chiefly upon the recognition of both clear and granular cell types; frequent tubular formations in the

tumor and often papillary projections and outgrowths such as are never seen in the normal adrenal cortex or in tumors derived from it.

Since 1893, therefore, the argument as to whether these tumors are of renal or adrenal origin has been continuous and has never really been definitely settled. For instance, MacCallum[4] states: "In the lack of any perfectly decisive proof it seems to me that *their arguments* (supporters of the renal origin) are not entirely convincing, and that the evidence which Grawitz himself brought forward to show their relation to the adrenals is stronger." Whereas Boyd,[2] in discussing the adrenal origin, states, "For long this was the popular view, but it must be given up, for there is no doubt that the tumor is a renal carcinoma arising either from adult tubules, or as suggested by Wilson, (Wilson and Willis[23] in 1911) from islets of nephrogenic tissue which have persisted in the renal cortex." Again, Karsner,[10] who strongly supports the renal origin of these tumors, avoids the issue by calling practically all of these tumors "Renal Carcinomas or Malignant Nephromas," which are grossly like carcinoma and microscopically like the clear-cell type. It is probably derived from adrenal remnants in the renal cortex. However, most authorities at present believe that the majority of these tumors are of renal origin, mainly because tubular structures are never seen in the adrenal cortex or tumors originating from this tissue, and that many of the so-called adrenal rests in the kidney are really renal adenomas springing from tubular renal epithelium. Nevertheless, Ewing,[7] has recently stated: "Yet the opponents of Grawitz's theory seem to have gone too far in practically eliminating the adrenal rest as a source of renal tumors."

Argument Based Upon Embryological Theories.—A great objection to the theory which attributes these kidney tumors to adrenal rests is the great distance between the adrenal and the metanephros or permanent kidney in early fetal life and also the development of a strong renal capsule long before the adrenal and kidney come into close contact. The adrenal cortex develops from mesoderm of the Wolfian ridge and the adrenal medulla from ectoderm of the primitive ganglionic crest, both organs far distant from the metanephros. Embryologists hold that the formation of the capsule of the kidney dates back to the latter part of the second month of fetal life. At this time the kidneys and adrenals are far apart. The

two organs do not meet each other before the middle of the third month, at which time of contact each organ possesses already a well developed capsule. It would seem impossible that a mechanical mingling of their tissues could take place at this time.

Furthermore, as Schiller[18] has recently pointed out, modern embrylogical concept tends to support a theory that in early fetal life, when the mesenchyma is still pluripotent, the matrix of the renal and of the adrenal cortex possesses the potency to differentiate into either renal or adrenal tissue. Schiller states if latent adrenal cortical potencies remain in the renal parenchyma cells, such cells, years later, may give rise to adrenal tissue. The presence of renal and adrenal potencies in the same cells may produce tissues of a hybrid type with combined renal and adrenal characteristics, such as Grawitz tumors with cystic and papillary structures corresponding to tumors originating from renal cortical tubules, but containing polyhedral fat storing cells resembling adrenal cortex. This is certainly the easiest and perhaps the safest way to explain the origin of these controversial tumors.

Argument Based Upon Functional Structures.—Schiller also called attention to the presence of numerous hyaline droplets in the cells of a Grawitz tumor when tubular structures were present, stating that they are similar to the droplets seen in the renal tubules in cases of nephroses. It is fairly well established that these droplets in kidney disease indicate the reabsorption of protein excreted by the glomeruli in the renal tubules. In addition, in the frequent areas of hemorrhage (often the cause of hematuria) in the Grawitz tumor, a similar reabsorption of the protein hemoglobin takes place.

Both of these observations strongly suggest to Schiller that such tubular structures when present in a Grawitz tumor indicate a renal origin.

Argument Based Upon Endocrine Disturbance and Chemical Assay.—The fact that cortical adenomas of the adrenal are often associated with sex disturbances (virilism), and that these symptoms are constantly absent in the renal hypernephromas, is undoubtedly a strong argument against the adrenal origin of these kidney tumors.

It should be remembered, however, that Cahill,[4] in ten cases of cortical tumor of the adrenal, pointed out that cortical adrenal ade-

nomas may occur without virilism and that neither cortin nor any masculinizing hormone has been demonstrated in them.

We might add also that cortical adenomas of the adrenal, of 1 to 2 cm. in diameter, are frequently seen in routine autopsies, and most of them have apparently shown no endocrine disturbances during life. Even large bilateral cortical adenomas occur without virilism.

Observations Which Tend to Support the Adrenal Origin of the Hypernephromas.—It will be noted, therefore, that while most of the evidence seems to support the renal origin of the renal hypernephromas, there is still room for reasonable doubt in many cases. Hence, any anatomical observations showing that the adrenals may sometimes be found beneath the kidney capsule in intimate contact with the kidney parenchyma, and that old-fashioned small adrenal rests, now thought by many to be of renal origin, may still be bits of misplaced adrenal tissue, tends to support the original Grawitzian theory.

For many years the urological and pathological services of the Newark City Hospital have been in close liaison with the Medical Examiner's Office of Essex County, which office performs some nine hundred autopsies a year. All interesting urological conditions seen in the examination of violent deaths and sudden deaths from suspicious or natural causes are called to our attention.

For several years in the routine performance of autopsies in this office, one of us has noted, that every once in a while, the *entire adrenal* or a *greater portion* of the gland is situated beneath the true capsule of the kidney, lying in close contact with the kidney parenchyma.

This unexplained anomaly has been encountered in eight *of the last 5,000 routine autopsies.* It was found in seven males and one female. The youngest was thirty-eight and the oldest sixty years of age. All had died suddenly from natural causes or as the result of some accident. The condition was always bilateral.

Since the anomalous position of the adrenal glands played no part in the death of the individual, this finding, while noted in the protocol, was not indexed. Therefore, the incidence in this series cannot be obtained with accuracy without perusing several thousand autopsy protocols. We are under the impression, however, that

the anomaly might be encountered some *two* to *four* times in every 1,000 autopsies.

We have not noted this anomaly in infants and children, but this series is comprised chiefly of adults.

SUBCAPSULAR RENAL ADRENALS

Adrenal-renal Heterotopia.—This term should be confined to the developmental inclusion of the entire adrenal cortex (complete heterotopia) or a large portion of the adrenal (partial heterotopia) beneath the capsule of the kidney, lying in intimate contact with the upper pole of the kidney, with absence of any adrenal tissue in the normal position. In our experience this anomaly is always bilateral.

This condition should not be confused with isolated small bits of adrenal cortical tissue frequently found in and beneath the capsule of the kidney and known for many years as "adrenal rests," nor should it be confused with similar appearing rests of renal origin (adenomas) often found in sclerotic kidneys.

True adrenal-renal heterotopia was first described by Klebs,[11] in 1876. After this, cases were reported by Grawitz,[9] Ulrich,[21] Radasch,[17] Miloslavich,[14] Apert and Vallery-Radot,[1] Weller,[22] Brites,[3] and others. The literature contains less than twenty cases.

Most of the cases have been examples of true complete or partial heterotopia with no adrenal glands to be found in their normal position. The heterotopic glands consisted entirely of cortical tissue except in those cases of partial heterotopia, when medullary tissue could sometimes be found in the extracapsular portions.

In three cases, in addition to the subcapsular adrenals, there were adrenals present above kidneys, in their normal position. Such duplication of an adrenal gland, with one of the pair heterotopic, must be very rare.

Report of Cases.—The essential statistical data of the eight cases of bilateral adrenal-renal heterotopia encountered in 5,000 routine autopsies are shown in Table I.

Sex.—In this series males predominate seven to one, which is in accord with previous reports that adrenal-renal heterotopia occurs chiefly in males. So does hypernephroma.

Other Congenital Defects.—In one case a network of Chiari (lace-like veil in right auricle), a supposedly rare, but not uncom-

mon minor cardiac anomaly, was present. This was the only associated congenital defect.

Effect on Life.—Except for one case, there are no indications that this anomaly has the slightest effect on the duration of life,

TABLE I.—EIGHT CASES OF ADRENAL-RENAL HETEROTOPIA (SUBCAPSULAR ADRENALS)

Found in 5,000 consecutive autopsies, by the Medical Examiner's Office of Essex County

Case	Sex	Race	Age Yrs.	Left Adrenal	Right Adrenal	Cause of Death
1	M	C	39	Partial	Partial	Auto accident
2	M	W	52	Complete	Complete	Coronary occlusion
3	M	W	47	Partial	Partial	Auto accident
4	M	C	38	Partial	Partial	Appendicitis. Death on operating table
5	M	C	60	Complete	Complete	Railroad accident
6	M	C	59	Complete	Complete	Hypertension. Sudden death
7	F	W	30	Complete	Partial	Hypertension. Sudden death
8	M	W	60	Complete	Complete	Coronary occlusion. Sudden death during black-out

Males	7	White	4	Youngest	38 years
Females	1	Colored	4	Oldest	60 years

seven of the cases dying as the result of accidents or from coronary atherosclerosis. In only one case (patient in Case 4, dying under operation for chronic appendicitis) was there any evidence of lymphoid hyperplasia suggesting a status lymphatic type of individual.

The anomaly neither shortened life nor was associated with tuberculosis or other debilitating infections and in no case was there any evidence of hypogenitalism.

All this is interesting since previous authors, on the supposition that the heterotopic adrenal is thin and hypoplastic, have called attention to the high incidence of status, the asthenic habitus, tuberculosis and early death. Miloslavich found lymphoid hyperplasia and the status constitution. Karsner stated that the condition is

usually associated with the thymico-lymphatic constitution. Weller has stated that "adrenal heterotopia is usually associated with a persistent thymus and other evidences of the thymico-lymphatic constitution, and frequently the asthenic habitus. . . . Most of the

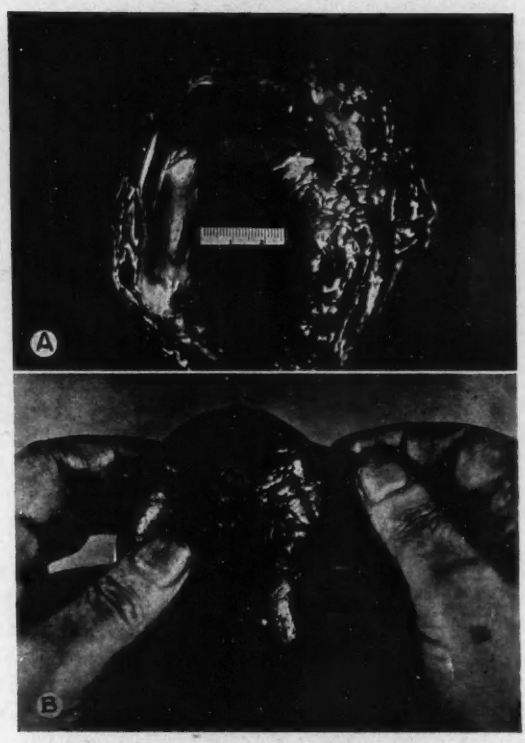

Fig. 1. *A*, Appearance of a subcapsular adrenal (complete heterotopia) as seen through renal capsule; *B*, same after stripping renal capsule. Note well formed adrenal gland remaining on kidney after decapsulation.

cases have died at a relatively early age. The incidence of tuberculosis and other infection is high."

Gross Appearance of Adrenals at Autopsy.—When the heterotopia is complete, these subcapsular adrenals retain, as a rule, the oval

or triangular shape of the normal adrenal. This can easily be made out even when viewed through the renal capsule (Fig. 1, *A*).

When the kidney is removed at autopsy the entire adrenal comes away with the kidney and no adrenal can be found above the kidney in its normal position.

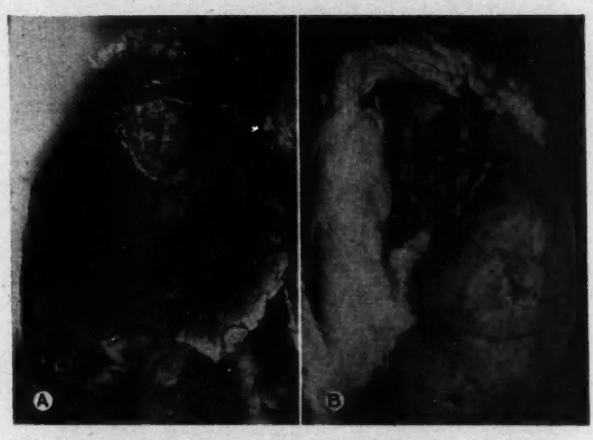

Fig. 2, *A*, Right adrenal; *B*, left adrenal in complete adrenal-renal heterotopia. Notes the well formed adrenal glands remaining on the kidneys after decapsulation.

On stripping the capsule of the kidney the yellow characteristic cortical adrenal is uncovered lying over the upper pole and anterior surface of the kidney and firmly attached to the kidney parenchyma so that usually no cortical tissue adheres to the capsule (Fig. 2).

Section of such adrenals shows that they are very thin and hypoplastic in spite of the fact that they cover a large surface area (Fig. 3, *A*). No medullary substance can be seen in complete adrenal-renal heterotopia.

The entire adrenal mass is often embedded in a shallow, saucer-like depression in the kidney substance from which it may be shelled out leaving bare kidney parenchyma (Fig. 3, *B*).

Sometimes in complete adrenal-renal heterotopia the adrenals consist of much smaller masses, which are irregular in contour and do not take on the shape of a normal adrenal. Frequently, small isolated masses of cortical tissue may be seen around the main adre-

nal mass, sometimes at a considerable distance from the adrenal (Fig. 4). Such small masses assume the characteristics of the so-called adrenal rests frequently found beneath the kidney capsule.

When the heterotopia is partial the inner subcapsular portion is similar to that seen in the complete type and lies firmly attached to

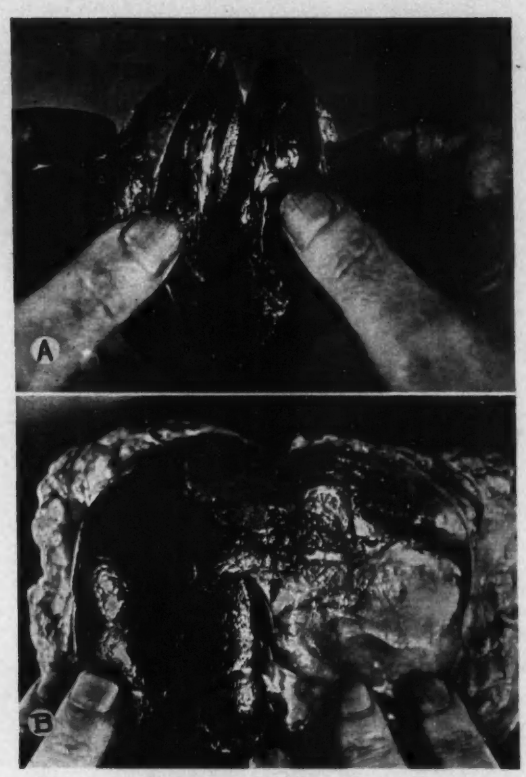

Fig. 3. *A,* Bisection of kidney illustrating extreme thinness of a subcapsular adrenal although its surface area is large; *B,* subcapsular adrenal firmly embedded in a shallow saucer-like depression in renal parenchyma.

the bare kidney parenchyma on stripping the capsule. The outer portion of the gland is often contained in peculiar folds of the renal capsule, frequently resembling diverticula and sometimes a

considerable portion of the gland may hang free and completely outside the capsule (Figs. 5 and 6).

The adrenal, however, is so completely involved in the renal capsule that it is entirely removed with the kidney and would undoubtedly be entirely removed in a nephrectomy.

Fig. 4. Complete adrenal-renal heterotopia with smaller, irregular masses of adrenal tissue beneath renal capsule. There were no adrenals above kidneys in this case. Note small, isolated masses of adrenal tissue scattered over surface of kidneys assuming the characteristic appearance of adrenal rests.

Medullary tissue can sometimes be recognized in portions of the adrenal which are entirely extracapsular.

The heterotopia may be partial on one side and complete on the other, or partial on both sides in any given case.

Blood Supply of Heterotopic Adrenals.—To the knowledge of the authors the arterial and venous blood supply in adrenal-renal heterotopia has seldom been worked out. It is unfortunate that more attention was not paid to it in this series, but the anomaly is usually not discovered until the pathologist has already removed the kidney. This should, however, be done on the opposite side, since the anomaly is always bilateral.

Adrenal-hepatic Heterotopia.—Occasionally the right adrenal in its entirety or a portion of the gland may be found beneath the

Fig. 5. A good example of partial adrenal-renal heterotopia. Note the small mass of cortical tissue embedded in kidney parenchyma beneath its capsule and a large portion of what appears to be normal adrenal entangled in renal capsule and protruding externally. Medullary tissue can sometimes be found in extracapsular portions.

capsule of the liver. We have never encountered this anomaly, but it could be easily missed unless carefully looked for.

Microscopic Examination of Heterotopic Adrenals.—In the complete type of adrenal-renal heterotopia the subcapsular gland con-

Fig. 6. Two examples of partial adrenal-renal heterotopia. The anomaly was bilateral in both cases. It may be partial on one side and complete on the other, or partial on both sides. Note in *A* how the adrenal is entangled in the renal capsule; and in *B*, how the subcapsular portion has torn out, leaving a saucer-like depression.

sists entirely of cortical tissue. No medullary substance was found in this series. There is usually no difficulty in recognizing all three

zones of cortex which have the normal architecture of the adrenal with normal distribution of capillaries.

The cortex, however, is quite thin when compared to the normal adrenal and is definitely hypoplastic.

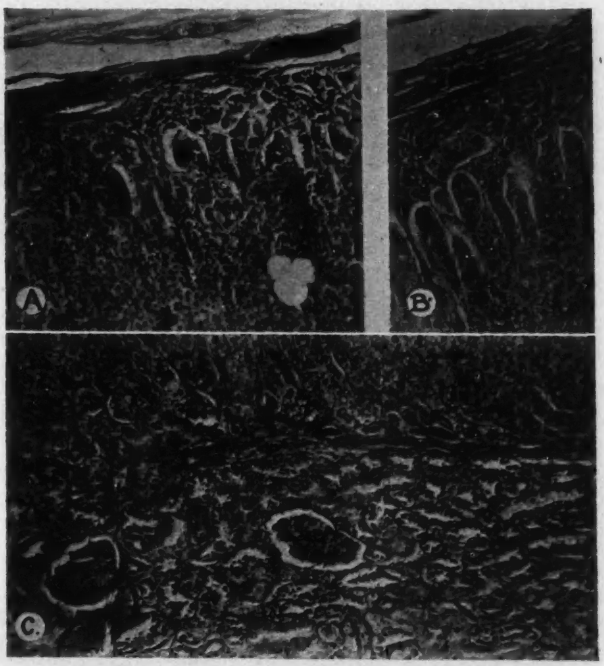

Fig. 7. Low power photomicrographs of complete adrenal-renal heterotopia. *A* and *B*, external surface of adrenal showing zona glomerulosa and fasiculata. The renal capsule has not been stripped off and is seen, in part only, as a dense fibroblastic capsule. *C*, Inner layer of cortex (zona reticularis) with absence of medullary tissue and thin, delicate connective tissue barrier separating kidney parenchyma.

A very thin connective tissue barrier can usually be made out between the inner layer (zona reticularis) and the kidney parenchyma. In many places, however, this is entirely absent and lipoid containing adrenal cells lie in direct contact with renal tubules and glomeruli (Figs. 7 and 8).

ADRENAL RESTS

Adrenal rests, accessory or misplaced adrenal tissue, are little yellowish bodies the size of a pin's head or slightly larger and have been found by pathologists for many years in the retroperitoneum,

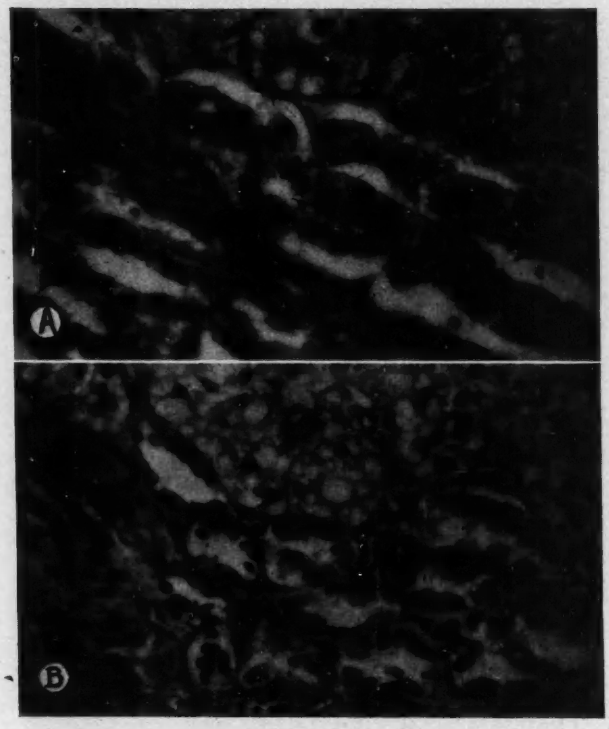

Fig. 8. High power photomicrographs of complete adrenal-renal heterotopia. *A*, Note very thin connective tissue strands separating adrenal from kidney below. *B*, Note absence of any capsule with adrenal cells above in contact with renal tubules.

under the capsules of the kidney and liver, in the space between the testis and epididymis, in the ovary and broad ligament, and especially along the line of descent of the sex glands.

They were first found near the adrenal by Morgani[19] in 1740

and by Marchand[20] in 1893 near the ovary and in the broad ligament. Chiari[21] in 1884 found them along the spermatic and ovarian veins, Daginet[22] in 1885 near the testes. Schmorl in 1891 told some one that he had found adrenal rests in about 92 per cent of bodies and that most of them were near the adrenal. Apparently this statement of Schmorl could never be verified and this high incidence has been greatly misquoted in the literature. Surgeons occasionally found these rests in hernia sacs during herniotomies.

Adrenal rests when examined microscopically are composed entirely of cortical adrenal tissue. These cortical rests are said to occur in fifty per cent of newborn infants and to rapidly atrophy and disappear. Medullary tissue is not found in these rests, but accessory chromophil tissue has been noted in the sympathetic ganglia and in front of the abdominal aorta.

It has been the opinion for many years that these rests were due to mechanical separation and displacement of portions of cortical tissue during migration and descent of the sex glands. They also may have a multiple primordial origin from pluripotent cells.

Recently Mitchell and Angrist[15] found these cortical adrenal rests in the kidneys of twenty-three cases in 2,896 autopsies and stated that "if the renal capsule is stripped carefully and the exposed surface of the kidney and its capsule minutely examined, the incidence of such foci increases markedly." In two renal hypernephromas these authors also found cortical adrenal rests in close proximity to the kidney tumor. This is of interest since many have long held that hypernephromas of the kidney originate from such cortical adrenal rests.

The correct interpretation of these rests is important since many of the supporters of the renal origin of all malignant adult tumors of the kidney have disputed the adrenal origin of many of these rests claiming that many are renal adenomas arising from renal epithelium and occurring chiefly in sclerotic kidneys.

Hypernephroma Arising From Extrarenal Adrenal Rests.—Proof that a primary tumor occurs which shows the characteristics of a hypernephroma while not being connected with either adrenal or kidney would greatly strengthen the argument that hypernephroma may rise from adrenal rests. A critical review shows that this is rare. We have seen but one case illustrating this possibility.

A man, white, aged thirty years, claimed to have injured his back while at work several months before death. Autopsy showed a large, primary tumor mass, 4 by 8 inches in diameter, in the retroperitoneum, just below left kidney and near lumbar spine.

On section, this tumor had the variegated appearance characteristic of hypernephroma: yellow, reddish-yellow and dark red areas with necrosis and marked hemorrhage. Microscopic examination showed the typical picture of hypernephroma. There were no tubular structures present.

The primary growth had finally extended into the left renal vein and there were numerous "golf-ball" metastases throughout both lungs.

The location of the tumor alongside of the lumbar spine in an area in which accessory adrenal cortical tissue often occurs suggests the strong possibility that the tumor originated in cortical adrenal rests.

SUMMARY AND CONCLUSION

Adrenal-renal heterotopia with the adrenal glands (complete heterotopia) or a considerable portion of them (partial heterotopia) beneath the capsule of the kidneys and with no adrenals in their normal position is not as rare an anomaly as the literature would indicate. We have encountered this condition eight times in the routine examination of five thousand consecutive bodies.

The explanation of this anomaly, which in our experience is always bilateral, is unknown. As the renal capsule is said to be completed at a time in early fetal life when the adrenal cortex is far distant, it would seem that a mechanical displacement is impossible. It suggests that either our embryological data are incomplete, that exceptions occur, or that pluripotent cells exist which can form either renal parenchyma or adrenal cortex.

Contrary to some authorities, this anomaly seems to have no effect on the life of the individual. In our experience it neither shortens life, nor predisposes to infections, tuberculosis or debilitating diseases. No endocrine disturbances were observed.

The recorded high incidence of status lymphaticus with this anomaly is not borne out in our cases.

In adrenal-renal heterotopia the surgeon in performing a nephrectomy would unwittingly remove the adrenal. We have never heard, however, that this has been done. Since the heterotopic adrenals are hypoplastic and, in addition, contain no medulla (or scant medulla in extracapsular portions only) such an operation might cause symptoms suggesting adrenal insufficiency.

Finally, the demonstration that the entire adrenal cortex, or large portions of it, may be found beneath the renal capsule remaining on the kidney after decapsulation; and the finding in some of these cases of many small, isolated bits of cortical tissue near these subcapsular adrenals, but scattered over the surface of the kidney, greatly strengthens the opinion held by many pathologists that the so-called adrenal rests are cortical adrenal tissue which have become misplaced during development.

It is reasonable to assume, therefore, that some renal hypernephromas may arise from such misplaced cortical adrenal tissue.

The only other explanation would be the concept that pluripotent cells exist which may give rise to any of these structures. There is no way of refuting such an argument.

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RENAL TRAUMA AND ITS RELATION TO HYPERTENSION

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The question has been raised as to what extent renal trauma may be a factor in hypertension of unilateral renal origin. Several cases have been reported in which a severe type of hypertension developed subsequent to renal trauma. Nesbit and Ratliff reported a case of hypertension in which removal of an injured kidney was followed by temporary lowering of the blood pressure, which suggested that renal trauma may have been the etiologic factor. Abeshouse also suggested renal trauma as an etiologic factor in hypertension.

In an effort to determine the relationship of renal injury to this type of hypertension, all cases with clinical evidence of previous renal trauma in the records of the Mayo Clinic were reviewed. Eighty-five cases were reviewed but thirty-five cases were excluded from further study. These included: (1) thirteen cases in which there was a renal lesion such as hydronephrosis, nephrolithiasis, pyelonephritis, nephritis and nephrosis and in which there was a doubtful history of previous renal injury; (2) six cases of abdominal trauma in which there was only presumable injury to the kidney; (3) thirteen cases of renal injury seen during the early years of the clinic when insufficient blood pressure recordings were made and (4) three cases in which the patients were in a state of shock prior to emergency nephrectomy performed immediately following renal trauma.

There remained fifty cases with a definite history of renal injury to a presumably normal kidney, in which the blood pressure was recorded at some time during the patient's examination at the clinic. Nephrectomy was performed in five of these cases. In forty-five cases, surgical treatment was not indicated.

COMMENT AND REPORT OF CASES

The forty-five cases in which no surgical treatment was indicated have been grouped according to the interval between the time of the injury and the time of the first clinical investigation following renal trauma. In twenty-five cases the patients were seen within

twenty-four hours after injury. In eight of these cases the blood pressure was normal and no subsequent recordings were made. In thirteen of the remaining seventeen cases the blood pressure was normal at the time of initial examination and when the patients were checked subsequently at periods varying from more than a year to nineteen years after the renal trauma, an elevation of blood pressure following renal trauma occurred in only two of the seventeen cases (Cases 1 and 2). These cases will be summarized briefly.

Case 1.—A boy, aged thirteen years, was brought to the clinic on December 29, 1933, complaining of gross hematuria and pain over the left kidney, subsequent to left lumbar trauma that had occurred the previous day while he had been skiing. Initial blood pressure readings were 150 systolic and 86 diastolic (recorded in millimeters of mercury). While he was in the hospital his blood pressure varied between 115 and 160 mm. systolic and between 40 and 86 mm. diastolic. An excretory urogram did not reveal any evidence of renal function on the left side.

Microscopic examination of the urine revealed hematuria grade 3 to 4 (on the basis of 1 to 4) during the first five days following injury. Eight years later (April 16, 1941) follow-up studies were made and the blood pressure varied between 128 and 160 mm. systolic and between 84 and 90 mm. diastolic. An excretory urogram revealed that the left kidney was not functioning and that it was atrophied. Cystoscopic examination revealed that no urine was coming from the left ureteral orifice. Indigo carmine was given intravenously but no blue appeared at the orifice of the catheter in the left ureter in twenty minutes. The left kidney was not removed.

The patient in Case 1 apparently had had hypertension prior to his injury since it would be impossible for the renal injury to cause hypertension within a few hours.

Case 2.—A boy, aged sixteen years, came to the clinic October 11, 1931, because of a right lumbar injury which had occurred the previous day. The injury had produced gross hematuria. The blood pressure was recorded as 140 mm. systolic and 80 mm. diastolic. When the patient was seen again nine years later (1940), his blood pressure was 160 mm. systolic and 100 mm. diastolic. At that time an excretory urogram was normal. However, eight years prior to the renal injury, when the patient had been only eight years of age, he had been examined at the clinic and his blood pressure had been 120 mm. systolic and 78 mm. diastolic.

It is evident that in Case 2 hypertension was already present during childhood, eight years before the renal injury. If none of the earlier blood pressure readings had been available, one might

easily infer that the renal injury might have been a factor in causing the increase in blood pressure. Apparently, however, the condition is one of so-called essential hypertension, which is occasionally observed in infancy.

In fifteen cases the patients were first observed from twenty-four hours to three months after renal injury. In six of these cases the only blood pressures recorded were those determined at the time of the clinical examination and in each case the pressure was within normal limits. In eight other cases in which the blood pressure was normal at the time of the initial examination, subsequent blood pressure recordings were available at periods varying from seventeen months to sixteen years following injury and these also were considered to be normal. One case (Case 3) in which the blood pressure was elevated following renal trauma will be reported in detail.

Case 3.—A man, aged forty-three years, came to the clinic January, 1938, because of bloody urine and backache which had been present since an automobile accident that had occurred twenty days previously. Examination revealed tenderness over the left renal region. The excretory urogram was essentially negative; cystoscopy was not done. Only microscopic hematuria was noted during several days of observation in the hospital. Blood pressure readings were 140 mm. systolic and 90 mm. diastolic. Twelve years before the renal trauma had occurred, the patient had undergone a subtotal thyroidectomy. His blood pressure at that time had been recorded as 165 mm. systolic and 88 mm. diastolic. He returned to the clinic eleven months later (December, 1938); his blood pressure was 180 mm. systolic and 110 mm. diastolic, and when he returned again, more than two years after the trauma (March, 1940), his blood pressure was 152 mm. systolic and 94 mm. diastolic. During the latter visits he was treated for exophthalmic goiter and it was found that his blood pressure was increased by the use of tobacco.

It is evident that in Case 3 the moderate elevation in blood pressure which persisted following renal trauma was continuous with a similar moderate hypertension previously noted. It could not be related to renal trauma.

There were five cases in which a diagnosis of renal trauma was first made at the time of clinical examination, three months or more following renal injury. In one of these five cases, mild hypertension was noted which, however, had been present prior to the renal trauma. In the second of these cases, renal injury had occurred twenty-nine years previously, and mild hypertension had been diagnosed by the patient's family physician but no study had

been made to determine the status of his kidneys or the cause of the hypertension.

In the third of these five cases, an elevated diastolic blood pressure was noted following renal trauma. In the two remaining cases, hypertension was present at the initial examination and persisted for many years. The last three of these five cases will be reported in greater detail.

Case 4.—A man, aged twenty-five years, came to the clinic in 1932 because of dull right lumbar pain which had been present since an injury had been sustained nine months previously when he had been struck by a baseball. Following the injury he had had bloody urine for two weeks. When he was examined at the clinic, urinalysis did not disclose any abnormality. Excretory urograms revealed right pyelectasis and caliectasis of slight degree, and apparently normal renal function in both kidneys. The value for the blood urea was 34 mg. per 100 c.c. The indigo carmine test revealed that differential function was normal in both kidneys. The retinal arteries were slightly narrowed. The blood pressure was 145 mm. systolic and 92 mm. diastolic. Nine years later (1941), a follow-up study revealed that the blood pressure was 155 mm. systolic and 100 mm. diastolic. An excretory urogram at this time revealed that the right kidney was essentially normal and ophthalmoscopic examination showed no changes in the retinæ. Differential functional tests were not made at this time.

The possibility that renal trauma was a factor in causing the hypertension in Case 4 may be considered. The fact that the increase in blood pressure was only moderate, as well as gradual, and the fact that the physical evidence of hypertension was minimal, might contraindicate this assumption. Elevation of blood pressure resulting from unilateral renal disease is usually much higher than was the blood pressure in this case. It is questionable whether this case could be cited as an example of posttraumatic hypertension. There was no clinical indication for nephrectomy.

Case 5.—A man, aged forty-two years, came to the clinic in 1918 because of a fall and blow over the abdomen, which had occurred two years previously and which had been followed by painless gross hematuria for eighteen months. During this interval there had been a short time during which right renal pain had been present. When he was examined at the clinic, his blood pressure was normal. Examination of the urine revealed microscopic hematuria, grade 4. Cystoscopic examination revealed that the blood was coming from the right kidney. The phenolsulfonphthalein test revealed an excretion of 15 per cent of the dye by each kidney in fifteen minutes. A right retrograde pyelogram revealed only a slight deformity and dilatation of the calyces and

renal pelvis. It seemed very questionable that gross hematuria would persist eighteen months following injury without some cystoscopic or urographic evidence of renal injury, and it would be logical to regard the condition present as an essential renal hematuria. The renal pelvis was irrigated with a solution of silver nitrate. Except for a few days, several months later, no further hematuria was noted. Twenty-five years later, his family physician reported that the patient's blood pressure was 180 mm. systolic and 115 mm. diastolic. No studies were made to determine the cause of the hypertension. The patient is now sixty-seven years of age.

The history of renal trauma and the presence of hypertension twenty-five years later at the age of sixty-seven may have been merely coincidental. If the renal trauma were a factor in causing hypertension, in all probability it would have been apparent within two years after injury.

Case 6.—A man, aged forty-three years, came to the clinic because of a crushing injury to the abdomen which had occurred six months previously and had been followed by hematuria which had persisted for five weeks. Pain below the right costal margin had been present since the accident. Examination revealed tenderness over the right renal region. The blood pressure was 130 mm. systolic and 95 mm. diastolic. A right retrograde pyelogram revealed slight caliectasis and areas of calcification in the cortex of the kidney which were believed to be posttraumatic. Cystoscopy revealed normal function and absence of infection in the right kidney. Subsequent blood pressure recordings were not made. The patient died six years later, presumably of a heart attack.

In the presence of a definite renal lesion following injury of the kidney, the elevated diastolic pressure may assume some significance. However, this is not the type of hypertension which usually accompanies pathologic changes in the kidney as described by Goldblatt and his associates.

In only five of the fifty cases of renal trauma suitable for this study did nephrectomy seem advisable at the time of clinical investigation. In keeping with generally accepted methods, we have found that conservative treatment of a renal injury is usually followed by recovery. Nephrectomy is found necessary in only a few selected cases. Nephrectomy was performed within a few hours after injury in one of the five cases. The preoperative blood pressure was normal in this case. In a second case in which renal injury had occurred four months previously, the preoperative blood pressure was normal. Of interest in this case is the fact that the kidney weighed only 80 gm. and showed complete infarction of approx-

imately two-thirds of its substance. Hypertension was noted following renal injury in three other cases (Cases 7, 8 and 9). In each case, nephrectomy resulted in the lowering of the blood pressure. These three cases will be reported in greater detail.

Case 7.—A boy, aged fourteen years, was referred to the clinic by his family physician because of hypertension. Three months previously he had fallen from a bicycle and had injured his right side. This had caused lumbar pain and gross hematuria. Examination revealed that the blood pressure was 146 to 160 mm. systolic and 80 to 94 mm. diastolic. An excretory urogram did not reveal any evidence of renal function on the right side. A retrograde pyelogram indicated apparent traumatic rupture at the right ureteropelvic juncture. Right nephrectomy was performed and the specimen revealed an infected hydronephrosis with almost complete destruction of the upper pole of the kidney due to trauma. One week later, the blood pressure averaged 115 mm. systolic and 70 mm. diastolic.

Although temporary lowering of blood pressure while the patient is still hospitalized is not conclusive, the postoperative reduction in Case 7 would support the conclusion that the injury of the kidney was the probable cause of the hypertension. Unfortunately, the patient could not be followed for subsequent studies.

Case 8.—A boy, aged seven years, came to the clinic because of left renal trauma that had occurred six and one-half weeks previously. The blood pressure on admission was 120 mm. systolic and 80 mm. diastolic, which might indicate an elevated blood pressure for a child of this age. Left nephrectomy was done and the specimen was described as showing pyonephrosis and acute diffuse nephritis following traumatic rupture. The patient returned six years later and the blood pressure was 110 mm. systolic and 80 mm. diastolic. At a later visit to the clinic, when he was fifteen years of age, the blood pressure was 118 mm. systolic and 70 mm. diastolic. These latter figures may be considered normal for the corresponding age of the patient.

This case might be cited as an example of posttraumatic hypertension with recovery following removal of the injured kidney; however, the possibility of temporary toxic or psychic factors causing a slight increase in blood pressure at the time of primary examination is not excluded in this case.

Case 9.—A young man, aged eighteen years, came to the clinic in 1942 because of a mass in his right side. Approximately eighteen months previously, while he had been playing football, he had injured his right side. He had thought the injury was trivial and had not observed any bloody urine. Six months later, he had noticed a mass in

his right side. Examination at that time by his family physician had revealed a systolic blood pressure of 170 mm. On examination at the clinic, the systolic blood pressure was 170 mm. and the diastolic pressure ranged between 100 and 110 mm. The retinal arteries were normal. An excretory urogram revealed a large mass in the region of the right kidney, and very little function of this kidney. A retrograde pyelogram was attempted but no contrast medium was seen above the region of the ureteropelvic juncture. Exploration of the right kidney on April 20, 1942, revealed a large cystic mass (13 by 12 by 10 cm.), which was found to contain 1,500 c.c. of old blood-stained fluid and to be incorporated within the renal capsule. Nephrectomy was performed. Pathologic examination revealed that the cyst was an old subcapsular hematoma and that the remaining renal parenchyma was the site of chronic pyelonephritis. Blood pressure recordings twice a day for the next seventeen days revealed that the systolic pressure varied between 118 and 158 mm. and the diastolic pressure varied between 64 and 100 mm. In January, 1943, nine months after nephrectomy had been performed, the blood pressure was 130 mm. systolic and 80 mm. diastolic.

Although the patient in Case 9 has not been followed long enough for any final conclusions to be drawn, it would appear from the nature of the lesion and the clinical course following nephrectomy that the renal injury was directly related to the development of hypertension. It would seem probable that the intrarenal tension was increased by pericapsular pressure similar to that observed with artificial perinephritis employed in animal experiments, as described by Page. The blood pressure in this case returned to normal following nephrectomy.

These three cases would seem to indicate that certain types of pathologic changes in the kidney may follow renal injury and cause hypertension, and that when the injured kidney is removed, the blood pressure returns to normal. It would seem that secondary infection is an important etiologic factor. It is of interest, however, that only three of the fifty cases were of this type.

A further attempt was made to determine the effect of an injured kidney on blood pressure in cases in which necropsy was performed. The autopsy records at the clinic were searched for cases in which there was a history of renal trauma but in which death resulted from causes not directly related to the renal injury. Those cases in which patients died without adequate blood pressure recordings before death and those in which the patients were in a state of shock just before death were excluded from study. Those cases in which a history of renal trauma was obtained but in which no demon-

strable lesion due to trauma was found in the kidney at necropsy also were excluded. There remained only four cases suitable for further study. Although there was demonstrable pathologic evidence of renal injury varying from circumscribed cicatrical changes to almost complete destruction of the kidney in the necropsy specimens, in none of these four cases was there evidence of hypertension prior to death or at necropsy. One of these four cases (Case 10) is summarized briefly. Apparently no secondary infection occurred in these cases. The cicatrical changes in the renal parenchyma could be explained by trauma.

Case 10.—A man, aged sixty-two years, complained of epigastric pain. Nine years previously he had been kicked by a horse in the right lumbar region and had noted gross hematuria on two occasions immediately following the injury. His blood pressure on admission was 150 mm. systolic and 82 mm. diastolic. The patient died of inoperable carcinoma of the stomach and pulmonary atelectasis shortly after his admission. At necropsy the right kidney was found to be much smaller than normal and weighed only 84 gm. There was a scar, 1 cm. deep, completely encircling the kidney, and the lower pole was greatly reduced in size. Otherwise, the renal tissue was normal. The pathologist in describing the specimen noted that this kidney apparently had been completely severed and subsequently had repaired itself.

SUMMARY

A review of fifty cases with clinical evidence of renal trauma would indicate that although renal injury may be related to hypertension it is not a common cause. Nephrectomy was performed in five of these cases. Hypertension existed in three of these five cases and, following removal of the kidney, the blood pressure returned to normal. In the other two cases, the preoperative blood pressure was normal. The small number of patients with renal injury who underwent nephrectomy would corroborate the value of conservative treatment.

In thirty-eight of forty-five cases in which no operation was indicated, the blood pressure was found to be normal subsequent to renal injury. In six of the other cases, the degree of hypertension was moderate and the hypertension either existed prior to renal injury or was explained by factors other than renal. In only one of these cases was renal trauma considered a possible factor in the production of hypertension.

It is apparent that the resulting changes in the renal tissue fol-

lowing injury usually do not cause hypertension. In those cases in which operation was not indicated, it is evident that the injured renal tissues either healed or that moderate, mild, circumscribed cicatricial changes resulted.

Hypertension due to renal trauma usually occurs in cases in which there is secondary renal infection. This is in keeping with the fact that changes in the renal tissues secondary to chronic infection have been noted in most renal lesions which are known to cause hypertension. There was one exception, however, in the case of a patient with hypertension who was observed nine months after injury, in whom an encapsulated hematoma was found compressing a large portion of the kidney without infection.

When hypertension exists following renal injury it may be difficult to determine whether the injury is an etiologic factor unless the blood pressure and other clinical records prior to injury are available.

In several cases the clinical records made prior to renal injury showed that hypertension had existed previously. Without these data, an erroneous conclusion might easily have been made.

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DISCUSSION

DR. CLYDE L. DEMING (New Haven, Conn.): I would like to congratulate Dr. Dodson for his application of the operation which I presented before this Society fourteen years ago. My feeling is similar to his, that there are many operations which can be applied to correct a nephroptosis, and I do not claim that this is the only operation that can be used successfully.

(Slide) I would like to show a photograph of an anatomical plate which I think explains the idea which I had originally, that when the kidney drops down between the two layers of renal fascia, all we are dealing with is a renal hernia, so to speak, and that if we can push the kidney up and close this hernial sac with the kidney in position, we have corrected the anatomical defect. By doing this, one does not in any way interfere with the capsule or the kidney itself, so that the procedure is simply a correction of anatomical derangement of the kidney.

(Slide) The operation, as I described it, allows a free lysis of the kidney and pedicle and the upper ureter. The fascia is in close proximation with the peritoneum, so that if one pulls the upper fascia over, one can often see through it into the peritoneal cavity and the liver edge. I do not think there is any harm in passing a needle through this, fastening the perirenal fascia to the posterior wall of the abdomen.

(Slide) The perirenal fat must all be removed. In many cases where there is a long, flat lumbar segment in the individual, one must make a pocket for the kidney. If sometimes the liver is low and there seems to be very little room, the kidney must be pushed up before the layer of mattress sutures is placed through the fascia.

(Slide) Care must be taken, of course, to avoid the ureter and the ascending colon. This is simply an elaboration and continuation of that layer.

(Slide) The support of this is amplified by bringing up the extraperitoneal fat and suturing beneath the other layer.

Now, I have been criticized for this operation because a patient developed a fistula of the ascending colon. I warned that care must be used in placing this suture under vision to avoid piercing the colon with the needle.

A short time ago, I was called to see a patient who was operated upon outside of New Haven unsuccessfully, for the patient was still having pain. She was again operated on, and the upper pole of the kidney was where the lower pole should have been—in other words, the kidney had been rotated 180 degrees. Care must always be used in placing the kidney in good position, leaving the ureter in a straight and free course.

The indications for the operation, I believe, have been pretty well signified. We feel that a diagnosis should be definite. We have been criticized for doing nephropexies on infected kidneys. I am glad Dr. Dodson brought that point out, because I believe it should be done in infected kidneys which have a normal function.

Dr. Hughes' kymography could be well applied in nephroptotic cases to support the diagnosis; although the emptying time may be only slightly shortened, the ureter may be at fault, or it may be kinked.

The failures which we have had have been only two, and Dr. Dodson mentioned one—that is, in general visceroptosis; and, in the second case, a case of abdominal adhesions. I think those are the two hardest cases perhaps to rule out, and those are the ones which I really feel should not have any type of nephropexy.

Dr. Leon Herman: In connection with Dr. Braasch's paper, I think it worth while to consider surgical injury as a cause of hypertension. We may have a partial answer to the problem in the person of a thirty-eight-year-old man who had a heminephrectomy for calculous pyonephrosis elsewhere four years ago, prior to which the blood pressure was said to be normal.

When I first saw this patient one year ago he had a small stone in the remaining segment of the kidney, associated with Staphylococcus aureus infection. The blood pressure at that time was 210/170. The stone came away spontaneously and the infection had disappeared. This patient's blood pressure remained exceedingly high and it seemed not to be of the essential type. Should the remaining segment of the kidney be removed? I think so.

I wonder if Dr. McKim's patient is really surviving on one-quarter of the normal renal tissue. It seems fair to conclude that the remaining kidney has undergone functional compensatory hypertrophy. If this is true, it is incorrect to assume that he is living on one-quarter of the total normal renal substance.

Furthermore, the term heminephrectomy is a misnomer in most instances since actually it is rare to remove half of the kidney in the physiological sense. It seems highly probable to me that Dr. McKim's patient has survived because the remaining portion of the kidney substance had undergone physiological and anatomical hypertrophy before the operation was performed. This in nowise dims the brilliance of the result.

DR. HUGH H. YOUNG: Dr. Dodson's careful report shows conclusively the great value of Deming's simple way of operating for nephroptosis. We have all been greatly intrigued by the simplicity of this technique, and have been waiting for a comprehensive report of late results. Dr. Dodson has indeed furnished definite proof that the simple method is effective.

Dr. O'Crowley's paper is one of the best that has been presented before this society for many years. His colored photographs of anatomical and pathological specimens are beautiful. The positive demonstration that considerable portions of the adrenal gland, in fact the entire adrenal, may lie beneath the renal fascia imbedded against the kidney parenchyma is very illuminating and important. This demonstration would seem to back up Grawitz' belief that hypernephromas of the kidney are of adrenal origin. Grawitz, however, described very small and multiple renal tumors which hardly seem similar to the inclusion of adrenal substance in the renal capsule, as shown by Drs. O'Crowley and Martland. I wish to congratulate Dr. O'Crowley and also Dr. Martland, whose laboratory in Newark Dr. O'Crowley took me to vist several years ago. Dr. Martland is certainly one of the most brilliant pathologists in the country, and his pathological museum is by far the best that I have ever seen. His preparations in color are remarkable, as is shown by the wonderful colored slides that Dr. O'Crowley has demonstrated.

Dr. Braasch's paper on hypertension is important right now when the operative treatment of hypertension is exciting such great interest. Dr. Braasch was one of the first to bring out the relation between chronic pyelonephritis and hypertension, and his note of caution is timely. Nevertheless, the possibility of hypertension being due to unilateral renal disease should be constantly before us, because by searching investigations, we occasionally will be able to

demonstrate that unilateral renal disease may be the cause of hypertension, and cure it by nephrectomy.

DR. MCKIM: I would like to state that Dr. Smith, my associate, deserves the major part of the credit for getting this through.

DR. C. RUTHERFORD O'CROWLEY: I want to thank Dr. Young for his remarks, particularly about Dr. Martland, because there are a great many men in this room who know him and know the genius he is. He is very appreciative and I am going to tell him how nicely you spoke of him. I am sorry he couldn't be here. His wife is desperately ill, or he would have been here.

DR. WILLIAM F. BRAASCH (Rochester, Minn.): It is difficult to give a definite answer to the question that Dr. Herman raised without further clinical data, but from what I can gather, reduction in blood pressure in his case might well be anticipated following nephrectomy. I am frequently asked to see patients with hypertension where there is a possibility of a unilateral renal lesion being the etiologic factor. In most of these cases it is debatable whether the hypertension is a so-called essential type of lesion or whether it is of unilateral renal origin. In some cases a renal lesion is present which might well be the cause of hypertension and all the other clinical data would indicate that the condition is a primary or so-called essential hypertension. A so-called surgical unilateral renal lesion may be present but it may be only coincidental and not etiologic. If there is a unilateral renal lesion present and there is some doubt as to whether the renal lesion is the etiologic factor of the hypertension, at the time the kidney is removed a unilateral sympathectomy is also done. Subsequently, a sympathectomy is done on the other side. Unfortunately, some of the results of nephrectomy will be obscured because of the sympathectomy performed simultaneously.

You will recall that when the subject of unilateral renal lesion and hypertension first came out, some enthusiastic observers reported that in 40 per cent of cases of hypertension which they saw, a unilateral surgical renal lesion was found. Subsequent observation has shown that unilateral renal lesions cause less than 1 per cent of all cases of hypertension observed. Nevertheless, the internist should consider the possibility of a unilateral lesion in every case of hypertension.

A factor in the detection of unilateral renal damage in some of the doubtful cases which is not sufficiently recognized is careful differential renal functional tests. Phenolsulfonphthalein offers the best method available for this purpose. Urography, cystoscopy and other tests may be negative, but if the phthalein output on one side, for example, is 30 per cent and on the other side only 10 or 15 per cent, a valuable clue is offered to an otherwise overlooked renal lesion—in fact, it may be the only evidence of a severe renal lesion.

THE EXPERIMENTAL USE OF VITALLIUM TUBES IN URETERO-INTESTINAL ANASTOMOSIS

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It was with high good hope that in April, 1942, we began the study of vitallium tubes in uretero-intestinal anastomosis in the dog. We approached the subject with three tentative hypotheses; if all proved true, then an improvement on the Coffey I method would be achieved.

The first hypothesis held that during the first five to ten post-operative days a partial interference with urinary outflow was occasioned by edema of the tissues at the anastomotic site between the ureter and sigmoid. If such an obstruction existed, though mild, secondary lowering of the kidney's resistance to infection might occur and hence infection either hematogenous or ascending would more readily follow.

The second hypothesis dealt with the nature of the healing of the anastomosis. We reasoned that if the ureter were held open by a prosthesis such as a vitallium tube until healing had become complete then the final orifice would be as large as the normal ureter and late stricture possibly obviated.

The third hypothesis was based on the preceding years' study which had shown that vitallium tubes in the urinary tract of the dog fail to become encrusted with deposits of salts.[1]

After some fourteen months of experimentation we believe that all three of the above hypotheses are false, and further, we feel that such findings should be reported in view of the original optimism which was held for vitallium tubes in the urinary tract.

METHODS

Large mongrel dogs (40 to 50 pounds) of both sexes were operated upon using soluble pentobarbital anesthesia and uretero-intestinal anastomosis carried out by means of the Coffey I technique with the modification that a small vitallium tube with a holder was inserted 1.5 cm. into the end of the ureter (Fig. 1). The distal half

The Austenal Laboratories of New York City supplied the vitallium tubes used in these experiments.

of the vitallium tube lay in the lumen of the sigmoid while the holder was placed between the submucosa and muscularis of the bowel. In this way the proximal half of the vitallium tube prevented collapse of the ureter in its passage through the wall of

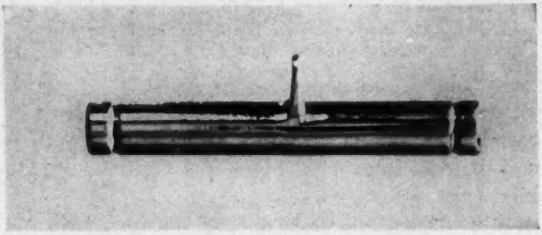

Fig. 1. The type of vitallium tube with holder used in this study. Its length is approximately 3 cm.

the bowel and the holder prevented the passage of the tube into the lumen of the bowel until the holder had eroded through the submucosa-mucosal layers.

The animals were operated upon in three series of experiments, the reasons for which will be given below.

RESULTS

In the first series of animals we performed, in two stages, uretero-intestinal anastomosis by the method described above. Twenty-six dogs were employed and thirty-six anastomoses carried out. Some of the animals failed to survive for the second stage. The

TABLE I.—SERIES I. THE COFFEY I METHOD MODIFIED BY THE USE OF A VITALLIUM TUBE ON BOTH SIDES IN TEN DOGS

No. of Dogs	No. of Uretero-intestinal Anasto-moses	Vitallium tubes		Good Results: Kidney, Ureter and Anasto-mosis
		Day passed, average	Calcification (0—4+)	
16	26	30 earliest 5 latest 82	average 3+ extremes {25 days 4+ {47 days 0	12 of 26

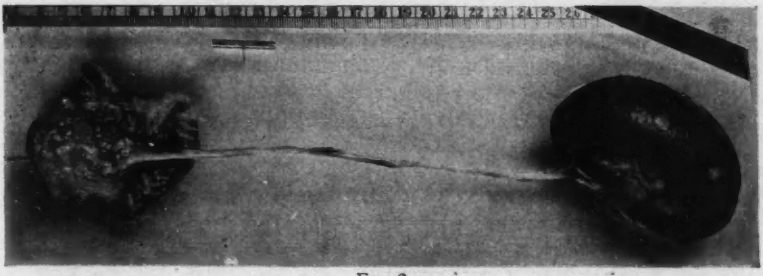

FIG. 2*a*

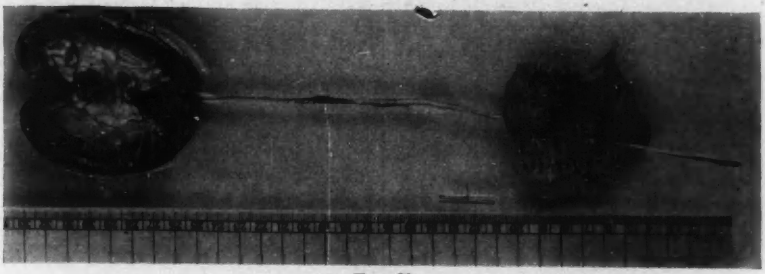

FIG. 2*b*

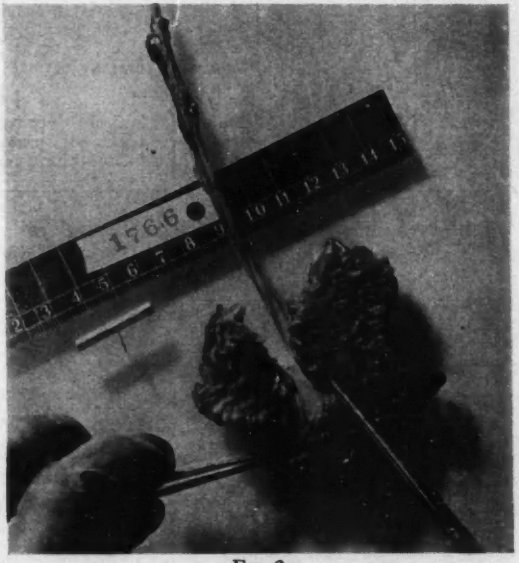

FIG. 2*c*

FIG. 2. *a* and *b*, Animal was sacrificed on the twenty-first postoperative day after a right uretero-intestinal anastomosis in which the modified vitallium tube technique was employed. The kidney and ureter are entirely normal. *c*, illustration showing excellent healing between the mucosas of the ureter and sigmoid.

results are shown in Table I. We found that there was a wide variation in the time when the vitallium tubes were passed and that calcification of some degree occurred in most of them, in general, proportional to the length of time they had been *in situ*. The long-

TABLE II.—SERIES II. COFFEY I METHOD CARRIED OUT ON ONE SIDE AND THE VITALLIUM TUBE MODIFICATION ON THE OTHER

Animal No.	Ureter	Method	Vitallium Tube		Result	Condition of Kidneys, Ureter and Anastomoses
			Day passed	Character		
2049	Right	Vitallium Tube	20	?	Excellent 23 days	Kidney and ureter normal; uretero-intestinal anastomosis well healed and patent
	Left	Coffey I			Poor 3 days	Animal died 3 days P. O. from acute pyelonephritis left. No hydronephrosis or hydro-ureter
2066	Right	Coffey I			Poor 22 days	Right pyonephrosis and hydro-ureter; stricture of right uretero-intestinal anastomosis
	Left	Vitallium Tube	0	No calcification	Good 1 day	Kidney, ureter and anastomosis in good condition. Died—bilateral bronchopneumonia
2058	Right	Coffey I			Excellent 48 days	Kidney, ureter and anastomosis entirely normal
	Left	Vitallium Tube	?	?	Excellent 26 days	Kidney, ureter and anastomosis entirely normal; vitallium tube not present. Died—bilateral bronchopneumonia

est time a tube remained in the operative site and failed to show any deposits was forty-seven days. In one animal in the third series complete calcification of the distal half of the tube inside and out had occurred by the ninth day.

The anatomical results in the first ten animals were so encouraging that the series was enlarged, only to fail to produce any conclusive answer to our first two hypotheses. Figure 2, *a*, *b* and *c* shows a well-healed uretero-intestinal anastomosis with a normal ureter and kidney above. There was excellent healing between the mucosas of the ureter and intestine.

A second series of three dogs was established in which on one

side a typical Coffey I procedure was carried out while the vitallium tube modification was performed on the other. Table II shows that in this small series the vitallium tube technique was more satisfactory than the Coffey I method but because of the untimely death of

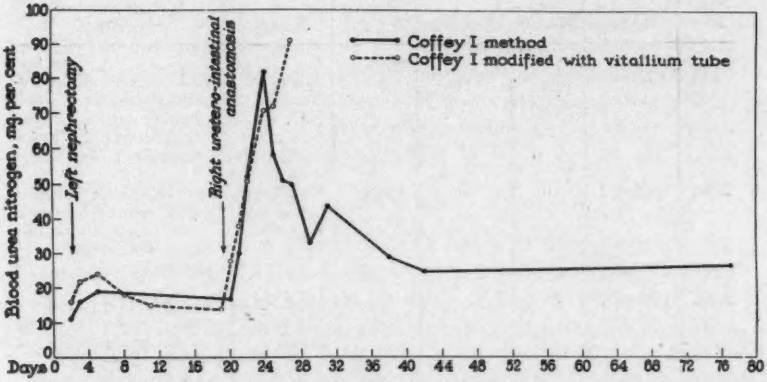

Fig. 3. Graph showing the average figures of the blood urea nitrogen of two groups of four dogs each following a left nephrectomy and subsequent right uretero-intestinal anastomosis. In one group the Coffey I method was employed and in the other group a vitallium tube modification was used.

two of the animals due to bronchopheumonia, a more crucial experiment was deemed necessary.

The third series was designed to settle conclusively the question whether the first two hypotheses were true or false. Eight dogs were subjected to left nephrectomy and some fifteen days later right uretero-intestinal anastomosis was performed; in four of these the Coffey I method was used and in the remaining four the vitallium tube method was employed. Blood urea nitrogen determinations were made at frequent intervals and, we feel, answer as well as possible, the first hypothesis. A graph (Fig. 3) shows the blood urea nitrogen results plotted in which the figures for the four animals of each group are averaged. As can be seen, there is a small and temporary rise in the blood urea nitrogen following left unilateral nephrectomy in all of the animals. However, after subsequent uretero-intestinal anastomosis on the right side exactly similar curves are obtained for the two groups. This finding would suggest that the rise in the blood urea nitrogen during the first five to six days

TABLE III.—SERIES III. FOLLOWING UNILATERAL NEPHRECTOMY, COFFEY I METHOD USED IN FOUR DOGS CONTRASTED WITH VITALLIUM TUBE MODIFICATION IN FOUR OTHER DOGS

Animal No.	Method	Vitallium Tube		Highest B.U.N.	Result	Condition of Right Kidney, Ureter and Bowel
		Day passed	Character			
881	Coffey I			mgm. % 61	Excellent sacrified P.O. 96	No infection; slight hydronephrosis; well healed patent uretero-intestinal anastomosis
2088	Coffey I			105	Excellent sacrificed P.O. 60	No infection; kidney and ureter normal; well-healed patent ureto-intestinal anastomosis
2090	Coffey I			70	Died P.O. 16 pneumonia	No infection; kidney and ureter normal; well healed patent uretero-intestinal anastomosis
2136	Coffey I			45	Excellent sacrificed P.O. 47	Urine grossly cloudy; kidney and ureter normal grossly. Well healed patent uretero-intestinal anastomosis
2082	Vitallium tube	20	Solidly calcified	98	Died P.O. 22 uremia	Pyonephrosis with dilated ureter; uretero-intestinal anastomosis healed and patent
2089	Vitallium tube	Not passed	Partially calcified	38	Died P.O. 14 multiple ulcers of small intestine	Moderate hydronephrosis without infection. Ureter normal and uretero-intestinal anastomosis healed and patent
2068	Vitallium tube	Not passed	Solidly calcified	97	Sacrificed P.O. 9 poor condition	Moderate hydronephrosis and hydro-ureter; uretero-intestinal anastomosis healed and patent; no infection
2174	Vitallium tube	Not passed	Slightly calcified	170	Sacrified P.O. 9 poor condition	Ureter kinked at lower end due to redundancy; moderate hydronephrosis without infection

is not due to interference with urinary outflow because during this period there can be no obstruction in the group with the vitallium tubes. The blood urea nitrogen in the four animals with the Coffey I procedure fell after the fifth day and gradually approached the preoperative level. When these animals were sacrificed the anastomosis was well healed, widely patent and the ureter and kidney above was normal in all animals. On the other hand, all four of the vitallium tube dogs died and varying degrees of obstruction were demonstrated at autopsy. In two of the animals obstruction was due to solid calcification of the vitallium tubes as the anastomoses were patent and well healed. (Table II.)

COMMENT

The third series of experiments, we believe, demonstrates that the first hypothesis, i.e., that edema at the operative site is associated with poor urinary outflow, is false, at least to the extent that such interference might be reflected in the postoperative elevation of the blood urea nitrogen.

The second hypothesis: the state of final healing of the anastomosis as influenced by the vitallium tube, found no positive corroboration in our experiments. In approximately 75 per cent of the vitallium tube animals perfect healing of the anastomoses occurred, whereas the Coffey I method achieved a considerably higher percentage of successful results in our hands.

Finally, the third hypothesis (that vitallium tubes rarely became encrusted in the urinary tract) was proven almost totally false where they contact a bacterially contaminated area such as the bowel over a period of several weeks. There are cases on record clinically where vitallium tubes have been used successfully in pancreatic and biliary duct drainage into the stomach and duodenum[2] over periods of months without obstruction. Therefore, the fact that in our experiments encrustation usually occurred on most tubes in three to five weeks would lead us to suspect that urine in association with bacterial contamination such as is found in the sigmoid is a combination which vitallium cannot withstand. The manufacturers† of vitallium believe that this has nothing to do with failure of chemical or electrical inertness of the alloy but rather is due to a mechanical factor in which deposits adhere to

†Austenal Laboratories, New York, N. Y.

the walls of the tube and lead to calcification with eventual occlusion. They express the opinion that any metal, no matter how inert, in this situation would be likely to gather calcified encrustation.

CONCLUSIONS

A modification of the Coffey I technique of uretero-intestinal anastomosis has been carried out in the dog by means of a vitallium tube inserted into the end of the ureter. The following conclusions have been drawn:

Suggestive evidence has been presented that the theoretical obstruction to urinary outflow caused by edema of the anastomosis is not the sole basis for the postoperative rise in the blood urea nitrogen.

Improvement in the late results of uretero-intestinal anastomosis of the Coffey I method by means of a vitallium tube was not obtained.

Vitallium tubes in constant contact with urine and the bacterial flora of the sigmoid usually became calcified in three to four weeks.

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TRANSPLANTATION OF THE URETERS INTO THE RECTOSIGMOID IN INFANTS

REVIEW OF NINETEEN CASES

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From the Cleveland Clinic, Cleveland

Exstrophy of the bladder, one of the most unfortunate of congenital anomalies, is a condition in which the anterior wall of the bladder and the corresponding portion of the anterior abdominal wall are absent. Thus the inner surface of the posterior bladder wall, partially everted, protrudes on the abdomen. Constant seepage of urine causes ulceration of the skin about the exstrophic bladder, and phosphatic incrustations and ulceration of the vesical mucosa may occur. As the children become older, they become social outcasts because of the odor from the constant dribbling of urine.

The symphysis is absent, as is the anterior part of the pelvic girdle, because the pelvic bones are not normally developed. In complete exstrophy the symphysis is separated for 2 to 7 cm., the intervening space being filled with connective tissues. This pelvic deformity accounts for the peculiar waddling gait in a child with this anomaly. Because of abnormality of the bony structures the recti muscles are widely separated below and are inserted into the pelvic bones by passing obliquely outward (Fig. 1).

INCIDENCE

Exstrophy of the bladder occurs once in approximately 40,000 births. The ratio in the male and female is seven to one. In this series of nineteen cases* of children under one year of age in whom transplantation of the ureters into the bowel and cystectomy were performed, twelve occurred in boys and seven in girls.

ETIOLOGY

Various theories have been advanced to explain the etiology of this anomaly. The hypotheses fall into three groups: (1) mechanical, (2) pathologic, and (3) embryologic. The *mechanical* theory may be divided into three groups.

*Series now includes twenty-two cases: Twenty of the children were discharged from the hospital in excellent condition. Two children died following operation.

1. The "berstungs" (rupture) theory explains exstrophy of the bladder and epispadias by rupture of the anterior wall and adjacent abdominal wall from retention of fluids in the bladder. This implies obstruction of the urethra or the vesical neck producing

Fig. 1

distention of the bladder, which by direct pressure separates the ends of the pubic bones and recti muscles. Eventually, the anterior wall of the bladder and the abdominal wall contiguous to it rupture, healing occurring along the edge of the exposed bladder. The so-called obstructive lesion responsible for the distention of the bladder has never been demonstrated.

2. The second mechanical theory incriminates an absent or short umbilical cord as the causative factor.

3. A third theory which is not exclusively mechanical states that the more complicated cases of exstrophy of the bladder are due to change in position of the vitelline duct.

The *pathologic* theory advanced by Keith states that toxins from an endometritis, or other forms of infection or irritation, produce a separation of the lateral walls of the caudal portion of the embryo.

Velpeau and Phillips believe that ulceration of the anterior abdominal wall involves the site of the symphysis pubis with subsequent necrosis and separation. Such ulceration, however, is not recognizable, and necrosis of the end of the pubic bones has not been observed in postmortem study.

Von Geldern states that "the arrest has affected those parts which had not completed their embryonal development, and that when development recommenced, certain primitive embryonal structures were maintained and developed as such, and those which should have undergone differentiation, had no arrest occurred, failed to make these changes."

Förster states that arrest in development is the causative factor in the production of simple exstrophy of the bladder and epispadias.

Johnston states that any explanation of this anomaly must consider the normal development of the bladder and lower end of the alimentary tract.† Complete exstrophy of the bladder complicated by intestinal openings on the extroverted area is caused by rupture of the cloacal membrane. The rupture may occur at any time between the first appearance of the membrane and the subdivision of the cloaca.

Keivel states that the anomaly may result from a persistent open blastopore.

Wyburn concludes:

"(5) At any early stage the cloacal membrane is a relatively large area of contact of ectoderm and endoderm extending some distance along the allantoic diverticulum.

"(6) The allantoic cloacal membrane is later obliterated by the mesoderm pressing in towards the midventral line between the ectoderm and endoderm.

"(7) Exstrophy of the bladder is due to mesodermal deficiency, particularly of the processes of secondary mesoderm arising from the hind end of the primitive streak, following on which there is persistence of the primary extensive cloacal membrane, impaired development of the muscular coat of the bladder, of the symphysis pubis, and the for-

†His case was a female fetus with exstrophy of the bladder complicated by the presence of intestinal openings. He concludes: "Epispadias is due to rupture of the urogenital part of the cloacal membrane at the site cephalad to the genital tubercle."

mation of the external genitals and the infra-umbilical portion of the anterior abdominal wall.

"(8) Epispadias is a similar mesodermal error in a minor form."

Thus many theories have been advanced to explain the etiology of exstrophy of the bladder, to which in many instances objections exist, although they may be minor. A firm foundation has been established, however, for further study of this congenital anomaly.

CLASSIFICATION

The four types of exstrophy of the bladder are as follows:

1. Fissura vesicae superior in which there is a normal union of the pubis but a defect in the upper part of the bladder.

2. Fissura vesicae inferior in which the symphysis is developed normally, but the bladder is split inferiorly.

3. Typical complete exstrophy in which the symphysis pubis is absent with varying degrees of separation of the pubic bones. The everted bladder protrudes above the level of the surrounding abdominal wall. Urine may be seen spurting from the ureteral orifices, and in older children the mucosa is inflamed. In the male epispadias is always present. The prostate may be absent, or cryptorchidism may occur. At times a bifid scrotum may be observed. In the female the clitoris is cleft, the labia rudimentary and the urethra forms an open sulcus. A double vagina or a bicornate uterus may also be present. Other anomalies such as atresia ani, hydrocephalus, spina bifida, cleft palate, and umbilical hernia may exist in both sexes.

4. Exstrophy of the bladder complicated by intestinal openings on the extroverted area. Johnston assumes a rupture of the cloacal membrane at an early period of embryonal development, with the exposure of the undifferentiated cloaca, to account for cases with intestinal openings.

From the literature it appears that there is an exstrophy of a retained cloaca. As stated by von Geldern, the retention of the embryonal structure is indicated by the complete absence of the large intestine and the presence of a mesonephric duct. Although the appearance of the cloaca changes comparatively little, those areas destined to form fetal structures show their intention by the character of their epithelial investment. The blind bowel which lies in the pelvis is usually present and has never been found in communication with the anus.

TREATMENT

Age of Patient.—The age for transplanting the ureters into the rectosigmoid for the relief of children with exstrophy of the bladder merits serious consideration. Without surgical intervention 50 per cent of the children die before the age of 10 and 66 per cent succumb before the age of twenty. In the majority of instances renal sepsis and renal failure are directly responsible for early death. It is usually advocated that operation be postponed until the child is four to six years of age and until he has gained control of the rectal sphincter.

This recommendation ignores the fact that children under five or six years of age experience repeated attacks of pyelitis or pyelonephritis, and in many instances death occurs before the child has attained four or five years of age. Obstruction frequently develops at the ureterocystic junction on the exposed bladder producing hydroureter and hydronephrosis, which may not only be conducive to upper urinary tract infection and destruction of renal parenchyma, but may render transplantation of the ureters into the bowel technically impossible or may in some instances necessitate removal of one kidney. Thus ureterocystic obstruction may produce stasis, followed by infection, renal sepsis, and impairment of renal function, resulting in death of the child during the first two or three years of life unless surgical intervention is advocated (Fig. 2). In view of results secured during the last three or four years, I believe that the operation should be performed in infants during the first year of life, preferably under six months of age, for the following reasons:

1. Just as the infant tolerates the trauma of passing through the birth canal, it tolerates surgical procedures quite well. As is attested by the results in other fields of surgery, delay is not countenanced; plastic operations for harelip, the Ramstedt operation for pyloric obstruction, operative intervention for intussusception or strangulated hernia, and other surgical procedures are performed without hesitation.

2. Recurrent attacks of renal infection may result in sepsis and death before the child is four to six years of age.

3. The organisms in the bowel of an infant under six months of age probably are less virulent than those in older children and adults.

4. Because of ureterocystic obstruction the ureter may dilate sufficiently to render its transplantation into the bowel technically impossible. Although one ureter may be transplanted, hydronephrosis on the opposite side may require removal of the kidney.

Fig. 2

5. If the operation is performed early in life, the child may develop normally both physically and mentally.

6. The operative mortality and morbidity are low.

7. The tone of the rectal sphincter, in my experience, has always been adequate to prevent leakage of urine from the rectum after the sphincter starts to function normally.

8. Because of the parents' attachment to the child, it is better that if a mortality should result from operation, it should occur before ties are established.

Pre-operative Preparation.—The purposes of the preoperative routine are (1) to cleanse completely the bowel of fecal content, and (2) to sterilize the bowel as far as possible.

Breast milk or formula is permitted, but no vegetables nor cereals are allowed. Rectal evacuation is accomplished by daily saline enemas. Sulfasuxidine, 0.25 gm. per kg. body weight, is given in six doses daily every four hours. If the child does not tolerate the drug it is discontinued. Additional vitamins are administered daily.

The foregoing preparation is given for four or five days prior to operation. On the day before surgery, only fluids in the form of glucose and water are permitted. Enemas are administered until the return is free of fecal content. Paregoric, ½ dram to ¼ dram according to the age of the infant, is given three times daily. A preoperative hypodermic of atropine is administered.

Operation.—The operation is performed under ether anesthesia. I do not recommend the simultaneous transplantation of the ureters into the rectosigmoid in infants under one year of age. The right ureter should be transplanted first, followed in ten days by transplantation of the left ureter into the bowel. The exstrophic bladder may be removed at this time. The plastic operation to correct the epispadias should be delayed until the child is five or six years of age.

Technically, transplantation of the ureter into the bowel is more difficult in infants than in adults. The diameter of the ureter in an infant is considerably less than in an adult, and the muscularis layer of the rectosigmoid is quite thin. The serosal and muscularis layers must be incised with extreme care down to the mucosa, therefore, to form the trough in the bowel wall to be occupied by the ureter.

A modification of the Coffey technique is used (Figs. 3, 4, 5). The anastomosis must not be too tight to prevent undue tension on the ureter with consequent kinking and angulation. The operation in reality is a plastic procedure, and it is my opinion that postoperative dilatation and hydronephrosis are due to technical errors and can be avoided. With intravenous urography the status of the ureters may be ascertained years after operation, and with refinements in operative technique dilatation of the ureters, so frequently observed in the past, is now infrequently seen.

No step in the operative technique is of more importance than

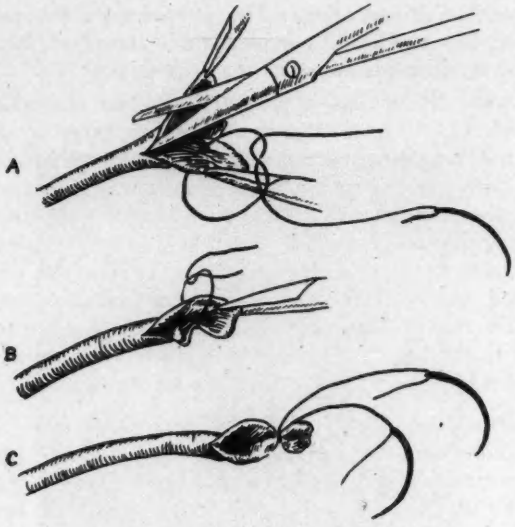
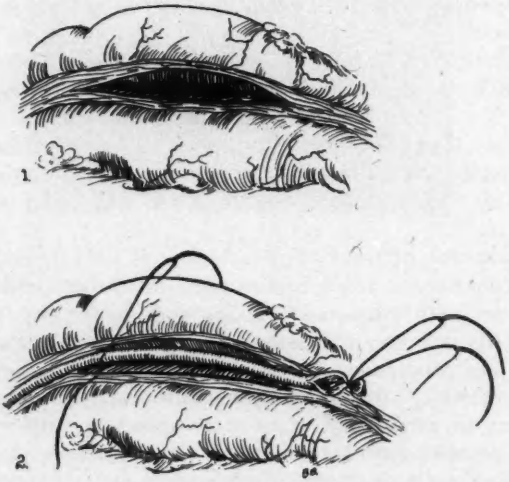


Fig. 3



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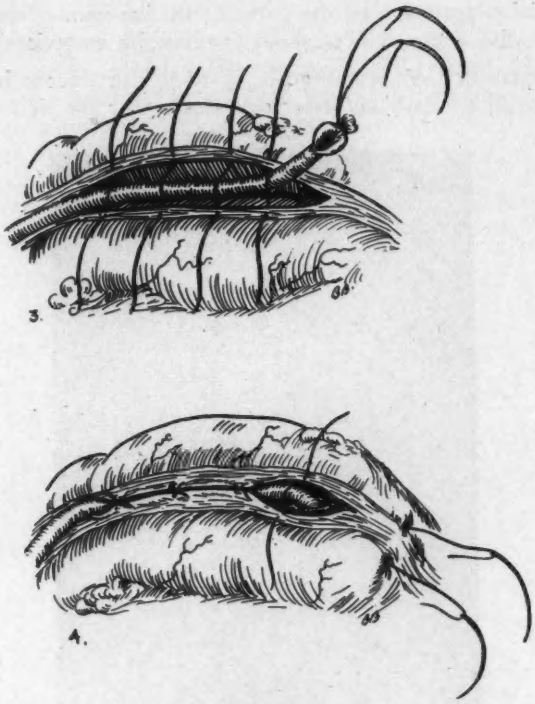
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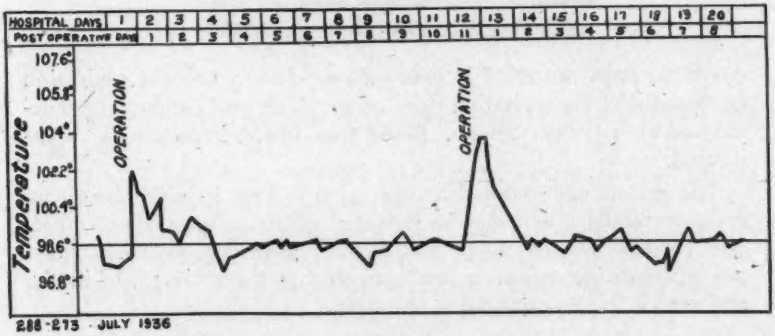
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Fig. 6

the initial preparation of the patient. In like manner an exacting postoperative regimen is essential to minimize complications.

Postoperatve Care.—Paregoric, ½ to ¼ dram according to age, is continued for one day after operation. For the first two post-

Fig. 7

operative days the child is kept on one side to prevent aspiration of vomitus if regurgitation does occur. The oral intake is supplemented by hypodermoclysis. Blood transfusion is performed if indicated.

The rectal tube inserted at operation is kept in place for from seven to ten days and may be irrigated gently at intervals to maintain patency of the tube. The diet is governed by the clinical course following operation, and an accurate measurement of intake and output is recorded daily (Fig. 6).

Complications.—In this series of nineteen infants with exstrophy

of the bladder in whom the ureters were transplanted into the rectosigmoid before one year of age, complications were negligible, and the postoperative course was smoother than in older children. In one case the wound disrupted on the sixth postoperative day. The

Fig. 8

complication has now been avoided by using silver wire to close the abdomen.

In a second case impetigo developed postoperatively but responded satisfactorily to treatment.

In two cases following transplantation of one ureter into the rectosigmoid and cystectomy, a nephroureterectomy was performed on the opposite side because of the presence of a large dilated ureter and an infected hydronephrosis. The causative factor was obstruction at the ureterocystic junction.

Mortality and End Results.—Two of the infants died following operation. On the third postoperative day one child vomited and aspirated the vomitus into the trachea. The second child died of bronchopneumonia following transplantation of the left ureter into the rectosigmoid.

The other seventeen infants were discharged from the hospital in excellent condition and are progressing very satisfactorily (Figs. 7, 8).

SUMMARY

Transplantation of the ureters into the rectosigmoid should be performed during the first year of life, preferably before the child is six months of age. This permits the operation to be performed before infection has been introduced into the kidneys. Postponement of the operation until the child is from four to six years of age will result in frequent deaths from renal sepsis. In other cases, because of repeated attacks of pyelitis, a subsequent pyelonephritis is present when the operation is performed. The postoperative course is unusually free of complications.

Obstruction at the ureterocystic junction may produce hydroureter which will render transplantation of the ureter into the rectosigmoid technically impossible if the operation is not performed during the first year of life.

In a total series of fifty-five cases in which the ureters have been transplanted into the bowel for exstrophy of the bladder, nineteen have been in infants under one year of age with the most gratifying end results in seventeen cases.

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LATE RESULTS FOLLOWING TRANSPLANTATION OF THE URETERS INTO THE RECTOSIGMOID

WM. E. LOWER, M.D.

From the Cleveland Clinic, Cleveland

When we recommend a procedure that will change the important upper urinary tract so that it functions into a structure alive with bacteria, the patient or the parents of the patient generally ask the question, "What about the future?"

For the immediate future we can promise them definitely that the risk of operation is very much reduced, because the occurrence of peritonitis, which was rather common in earlier operations, is now practically eliminated. Until one has followed a sufficiently large series over a long enough time, one cannot state what the social and economic status of the patient will be years later. A single isolated case may point the way, but hardly establishes the rule. However, we now have a series of cases which has been followed for more than twenty years, and we can answer this query with much more assurance. Out of eighty patients in whom the ureters were transplanted for non-malignant reasons, it is my desire to report herewith six who have survived for more than twenty years.

As we are now operating on this condition while the patient is still an infant, we have a relatively better chance of following these patients for a longer period than those which were operated upon as adults. Since 1932, when I first transplanted the ureters in a child five months old, we have advised the operation on infants.

I am including in this series of eighty cases only those that were operated upon for exstrophy of the bladder, vesicovaginal fistula, Hunner ulcer, and so forth; in other words, those cases of urinary incontinence which could not be corrected in any other way. This series does not include those operated upon for malignancies, for the prognosis is entirely different from the cases operated upon for a benign condition. I might mention, however, one case in which ureteral transplantation was done for a malignant tumor of the bladder: Total cystectomy was performed, and the ureters transplanted into the rectum. This patient, a doctor, is living and well after nine years.

After trying out various techniques we have reduced the opera-

tion to the simplest possible form by using only absorbable ligatures and no mechanical aids whatsoever.

There are certain points which, from our experience, should be emphasized. The first, of course, is the careful preoperative preparation of the bowel. Adults receive a nonresidue liquid diet. Magnesium sulfate, 1 ounce in 8 ounces of water, is given every morning daily in 1 ounce doses every fifteen minutes until the 8 ounces has been taken. The patient receives a daily cleansing enema. The day before operation no magnesium sulfate is given, but cleansing enemas are ordered as frequently as necessary to cleanse the bowel completely of any fecal material. Tincture of opium, 10 minims t.i.d., is given on that day. The pre-operative preparation should take between four and five days for complete emptying of the bowel contents. In addition, sulfasuxidine, 1 gm. every four hours, four doses daily, for four days is given pre-operatively. By this means we accomplish a double purpose: first, mechanical cleansing of the bowel, and, second, an attempt at sterilization of the bowel.

In infants daily cleansing enemas are given, but no magnesium sulfate is used. The diet consists of whole milk or milk formula, but no vegetables nor cereals are allowed. The pre-operative preparation lasts for three or four days. On the day preceding operation glucose water and water are substituted for the milk. Similarly, on the day before operation as many enemas are given as are necessary to obtain a clear return from the colon. On the day before operation ¼ to ½ dram of paregoric is given three times daily, the dose depending upon the age of the infant. Sulfasuxidine is given in amounts again depending upon the age and weight of the child.

Secondly, one must be especially careful to avoid angulation or constriction where the ureter is brought out from behind the peritoneum and is first attached to the bowel. Cases in which the ureter is transplanted for a shorter distance seem to do better than those in which the trough is too long and too much ureter is transplanted.

In adults, unless there is a contra-indication, we prefer to use spinal anesthesia as it more completely relaxes the abdominal muscles than an inhalation anesthetic, but in infants we generally give ether. In a number of cases both ureters have been transplanted at one procedure; this I believe, is without any particular risk, espe-

cially in adults, unless there is some condition which might prolong the operation.

CASE REPORTS

Case 1.—A girl, aged ten, was operated upon for exstrophy of the bladder. She had had a previous plastic operation without any benefit. In two stages the ureters were transplanted into the rectosigmoid. This was in 1921. The postoperative course was without serious reaction. During the years since then she has had a number of episodes of recurrent renal infection. During the past two or three years these attacks have been kept at a minimum by the use of the sulfonamides. Urograms have been taken repeatedly; the last in 1943, twenty-two years subsequent to surgery, showed prompt function from both kidneys and no evidence of either hydro-ureter or hydronephrosis. Her blood urea determination was 48 mg. per cent. This patient was employed at the Clinic and was kept as a control for ten years, from 1933 to 1943. She has been married for about a year, does her housework, and feels quite normal.

Case 2.—This patient was operated upon at the age of three and one-half years for exstrophy of the bladder. Ureteral transplantation was done in two stages in June and July, 1923. Neither surgical procedure was followed by any complication.

Beginning in 1939 several attempts were made for plastic repair of the hypospadias in order to produce a normally functioning organ. Plastic procedures were fairly satisfactory, and urethral dilations have been performed in order to maintain a channel sufficiently wide for passage of ejaculation.

Associated with his renal problem there is left hydronephrosis which, however, empties fairly well. The right kidney is normal, but there is some dilatation of the ureter. In 1939 his blood urea was 51 mg. per cent. He is in college taking a course in pharmacy. He is active in athletics and seems perfectly normal. The operation was performed just twenty years ago.

Case 3.—This man was operated upon at the age of twenty-three for exstrophy of the bladder. Bilateral ureterosigmoidostomy was performed in two stages, twelve days apart, in April, 1922.

He was last seen in March, 1943, twenty-one years later, and appeared rather feeble and somewhat infirm. A urogram showed poor initial function. In forty-five minutes the right kidney was visualized and showed hydronephrosis, whereas on the left side relatively little dye was seen. Despite this, however, his blood urea was only 51 mg. per cent. The patient stated that he had never been especially well, but he was sure he had been much better following the operation. We did not know the condition of his kidneys prior to operation, but the ureters were dilated.

Case 4.—This man was operated upon at the age of twenty-two for exstrophy of the bladder. A bilateral ureterosigmoidostomy was performed in two stages, twelve days apart, in April, 1922.

The patient was last seen in February, 1943; he looked perfectly well and felt fine. He was absolutely symptom free. He was very active, and it was my impression that he was perhaps the most comfortable of any of the patients we have followed for such a long period of time. His urea was 42 mg. per cent, and an intravenous urogram checked very favorably, showing normal kidney pelves.

This patient has been married for a number of years, is a very successful business man, and is now in the U. S. Signal Corps, Civil Service.

Case 5.—This woman was operated upon at the age of thirty for exstrophy of the bladder. Bilateral ureterosigmoidostomy was performed in two stages in October and November, 1921. A right inguinal herniorrhaphy was done with the second transplant. Interestingly, this patient consulted me relative to the hernia and not regarding the exstrophy for which she believed nothing could be done.

This patient was last seen in 1939, at which time an intravenous pyelogram disclosed a nonfunctioning right kidney, but the left appeared to be functioning quite well. Her blood urea at that time was 54 mg. per cent.

Also of interest is the fact that this patient married, became pregnant in 1939, but was advised to have a therapeutic abortion because of a high blood urea. This was done elsewhere. A written report from her in March, 1943, states that the patient is feeling well, is "fat," working hard, and is doing housework for folks besides farm work.

Case 6.—At the age of seven this patient had a bilateral ureterosigmoidostomy performed in 1916 (twenty-seven years ago), in two stages. When he was seen again eighteen years later, in 1934, he was found to have an infected hydronephrosis on the left. No further follow-up was advisable. In 1934 the blood urea was 36 mg. per cent. At that time the patient found it necessary to empty his rectum six or seven times during the day and two or three times at night. There was some difficulty in controlling the rectal sphincter, and he had a 4 plus Wassermann.

When last seen in April, 1943, he looked well and had better control of the anal sphincter which may have been due to the luetic treatment he had been getting. His blood urea was 54 mg. per cent, and an intravenous urogram showed a normal right kidney with hydro-ureter. The left kidney was not visualized.

As these patients were operated upon before excretory urography came into use, we do not know what the renal condition was before operation.

I might also mention that we have two patients who have gone

slightly over fifteen years since operation; both are married, and their social and economic status has been restored to an average normal.

CONCLUSIONS

Six cases are presented in which the ureters were transplanted into the rectosigmoid more than twenty years ago, and one twenty-seven years ago. Three are married, and none have been divorced. Their social and economic status has been restored.

We recommend the simplest form of operation as the best.

We advise the operation much earlier than formerly, when the patient is under one year of age.

DISCUSSION

DR. GEORGE G. SMITH: I can't refrain from congratulating Dr. Lord on the remarkably clear and concise way in which he presented his paper. I think that is the ideal method of presentation. I also think he and Dr. Stevens are to be congratulated on presenting a negative result. It saves a great deal of grief and experimentation on the part of others who might feel that that would be a very good way of treating some of these patients.

Dr. Higgins' results have been remarkable. I would like to see him do this operation; sometime, I hope I shall.

Dr. Lower's reports have been very interesting to me because I have been interested in this subject for a long time. I notice that he found the nonprotein nitrogen to be definitely elevated in a number of cases. I have seen that in some patients whose output of intravenous diodrast seems to be good, which makes one wonder whether there isn't an absorption from the intestinal tract of the nitrogen in the urine that tends to hold up the blood figure. That may not be so. I have some patients who have a perfectly normal N.P.N. I would like to know what Dr. Lower thinks about that.

DR. A. I. DODSON: I am extremely interested in this group of papers. I have had a very small series. Two of my patients have been operated upon for fifteen years and one eight years, all three of whom are living and well. One of these had an intravenous pyelogram made three years ago, which showed normal kidneys. He graduated from high school last year and is in every way an entirely normal boy. A colored boy that was operated upon eight years ago because of bilateral hydronephrosis and a contracted bladder is now entirely well. We did a bilateral drainage of the kidneys and after a period of time transplanted his ureters. I lost track of him until about three months ago he showed up at one of the induction centers in Richmond for induction into the Army. He had been living a normal life as a farm hand.

Dr. Higgins' paper is extremely interesting. I have had no opportunity to operate upon such young infants. I transplanted the right ureter of a two-year-old child two months ago. He developed a cold and returned home to come back in thirty days. Now, after

two months, he has not returned. I recently saw two infants that were delivered in a Richmond Hospital in the same week. I advised operation, but a general surgeon with urological inclinations came by and expressed the belief that he could develop functioning bladders for them. They are waiting for this possibility.

DR. REED M. NESBIT (Ann Arbor, Mich.): I, too, wish to congratulate Dr. Lord for his excellent paper and wonderful presentation. I want to affirm the statement made by Dr. Higgins about operating on children early. Since he made the suggestion, we have had an opportunity to operate on seven children under the age of four months, the earliest at the age of one month, the second-stage procedure being done at seven weeks in that particular case. I think these children are not too difficult to operate upon. I certainly agree with him.

There is one point that I would like to emphasize. I know that both Dr. Higgins and Dr. Lower emphasize it in their discussions, even if they didn't as they read their papers. The simplicity of operation, I believe, is very important. As Dr. Higgins showed in his pictures of the operation, there is only one layer of sutures over the anastomosis. So many times I have seen men perform ureteral transplantation in the human being, and in their anxiety to make this a good anastomosis, they have put in a second line of sutures. I think it is not only undesirable but also distinctly disadvantageous.

I would like to put on record here a case of a girl, upon whom I operated. She was nineteen years of age at the time of her transplantation of both ureters, four years ago. She became pregnant and delivered a stillborn child at about five months within a year after her operation and subsequent marriage. Just a year ago now she delivered a normal child by the birth canal.

There is one question I would like to ask both the essayists and others who may have an answer to it. During the last year we have seen three different children with exstrophy of the bladder and with prolapse of the anus or rectum. We just don't know how to handle that situation. I wish somebody would advise me.

DR. HUGH H. YOUNG: Dr. Lord is to be congratulated for giving us this frank paper in which he has demonstrated conclusively that tubes of vitallium cannot be successfully employed in operations upon the ureteropelvic junction or elsewhere in the urinary

tract. The demonstration that they rapidly become encrusted with urinary salts is very timely and important.

Dr. Higgins' demonstration that babies may be safely operated on a few days after birth is interesting. His ability to find the ureters in these tiny subjects and successfully transplant them into the bowel is a surgical triumph.

I wonder, however, whether Dr. Higgins' assertion that unless the operation is done promptly in cases of exstrophy, the ureters will rapidly dilate and become infected is generally true. I have seen a good many cases of exstrophy of the bladder in which the patients have grown to adolescence, even to twenty or thirty years of age, and there has been no evidence of serious renal back pressure. Dr. Lower has just told me that of the twenty cases in adults upon whom he operated for exstrophy, in only two of them were the ureters found dilated when the transplantation was done. It, therefore, would seem not absolutely essential to operate upon these babies immediately and safe to wait until a later date when perhaps the exstrophy could be cured by operation and urinary control obtained by appropriate plastics done at the same time upon the new formed vesical neck and penile urethra. The fact that it is possible to cure exstrophy was first shown by me in a paper in *Surgery, Gynecology and Obstetrics* (v. 74, pp. 727-737, 1942). The patient (BUI No. 28229), now aged eight years, has good urinary control. Since then I have had a boy aged eight years (BUI No. 28077) in whom an equally good result was obtained. I have now in the hospital two more boys in whom the exstrophy has also been cured by using fascial transplants. It seems probable that normal urination will be established in these two cases also. With these four successful results, I feel more and more justified in advising plastic operations directly upon the bladder and urethra to cure exstrophy and obtain perfect urinary control rather than to carry out the mutilation of removing the entire bladder after transplantation of the ureters into the bowel.

As you know, many surgeons have been frankly advising and carrying out removal of the bladder and transplantation of the ureters into the bowel in cases of epispadias. The operation for epispadias with incontinence is not a difficult plastic procedure, and I believe that the wholesale use of ureteral transplantation and sacrifice of the bladder in these cases are absolutely unjustifiable. A

number of these boys with epispadias and incontinence, upon whom I have carried out my plastic procedures, have now grown to adult age, and not only have normal urination but normal sexual powers, and one has produced two children.

DR. CHARLES C. HIGGINS (Cleveland, Ohio): Certainly I do not think you would be justified in re-implanting the ureters into the rectosigmoid with the presence of a prolapsed anus. I think the first procedure should be surgical correction of the prolapse and determination of the adequacy of the sphincter. I have not seen that complication myself, but it seems to me that I remember a case that Doctor Lower had years ago, in which he operated on the prolapse and later re-implanted the ureters into the bowel.

It is my impression that dilatation of the ureters is much more prevalent than we have suspected.

Now, in this series of nineteen infants, intravenous urography revealed definite indications of obstruction in seven instances. In two instances, the ureter and kidney had to be removed. I think the reason that Doctor Lower found normal ureters in the patient twenty years old is because those with dilated ureters and infection had died, and he saw only the ones who hadn't developed the obstruction.

The symphysis is always absent in the presence of a complete exstrophy—always.

DR. WILLIAM E. LOWER (Cleveland, Ohio): Perhaps the reason why we don't find many cases of dilated ureters in the adult is because most of the children who have them develop an upper urinary tract infection and die before they reach the adult stage.

Of course, we do not advocate transplantation of the ureters for epispadias unless we fail to correct the condition by plastic operation, and no one has done better work with good results than Dr. Young. He is certainly an expert on correction of the anomalies of the external genitalia.

Immediately following transplantation of the ureters, we often find temporary dilatation of the pelves and calices; within a month or six weeks they generally return to normal. I do not believe that excretory urograms are a true test of kidney function. Recently, we saw a case in which excretory urogram showed a nonfunctioning kidney, but retrograde catheterization of the ureter a few days fol-

lowing this returned a perfectly normal flow of urine from the kidney, so that we do not accept the evidence of a nonfunctioning kidney from one excretory urogram as final.

The principal indication for ureteral transplantation is an incontinence which cannot be corrected in any other way. Of course, the most common cause is exstrophy, and I doubt whether that incontinence can be corrected by simply doing a plastic operation on the bladder.

In reporting these cases which we have followed over a period of years, we are sure we have restored the economic and social status of these patients. As to just how long patients may live, we don't know, but as shown in the presentation, a number have gone for a period of twenty years and more in good physical condition.

TUMOR OF THE TESTICLE; ANALYSIS OF THE RESULTS OBTAINED IN FIFTY PATIENTS TREATED BY X-RAY THERAPY

GEORGE GILBERT SMITH, M.D.

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The necessity of irradiating the lymph nodes to which metastases from the malignant testicle most commonly extend has been questioned. Because of this fact, and because it seemed desirable to check up on the results obtained in the Tumor Clinic at the Massachusetts General Hospital, a study has been made of fifty patients with cancer of the testicle.

The greater part of the material has been found in the records of the above clinic; a few cases have been added from the Huntington Hospital, from the Palmer Memorial Hospital and from our private practice. The period covered extends from 1928 to 1943. The ages of these patients are given in Table I.

In all but two of these patients, orchidectomy was done as early as possible. We have not followed the procedure advocated by the Memorial Hospital, of giving a preliminary course of irradiation to the testicle. The value of an early diagnosis has seemed to us to outweigh the possible advantages to be gained from irradiation before orchidectomy.

The diagnosis was either teratoma or embryonal carcinoma in all cases. Certain pathologists prefer the former term and appear to employ it when other pathologists would use the latter. We have not found the distinction to be of practical value, although we realize that, generally speaking, a teratoma contains a larger proportion of mixed elements. Careful search has shown that these elements are present in tumors which appear to be composed of cells derived from a single embryonic layer.

One patient had an embryonal carcinoma of the epididymis. The others involved the testis itself. There were two chorionepitheliomas, both of which were rapidly fatal. Two patients had bilateral tumors; in one, the left testis had been removed nine years before the right was found to be affected. The exact pathological diagnosis of the earlier tumor was not known. The other patient had both

testes removed at the same time; both proved to be embryonal carcinoma.

There are several points in regard to the preoperative examination of these patients which should be considered. In addition to the examination of the tumor itself, there should be careful search

TABLE I.—FIFTY CASES OF TUMOR OF TESTICLE

Age at operation		
Under 20	3	(youngest 16)
20-29	7	
30-39	17	
40-49	7	
50-59	9	
60-69	5	
Not given	2	
	50	

for metastases. The condition of the supraclavicular gland should be noted. If it is enlarged, there is a three to four chance that the mediastinum or lungs also contain metastatic deposits.

A chest film should be examined for widening of the mediastinum and for the small circular areas of consolidation in the lung fields which indicate pulmonary metastases. A flat radiograph of the abdomen may show the existence of a mass located close to the spine in the upper abdomen. Intravenous pyelograms are desirable. In nineteen of our fifty patients excretory urograms were made; thirteen showed no abnormality but two showed unilateral hydronephrosis, one bilateral hydronephrosis and three showed a nonfunctioning kidney. These radiographs are helpful not only in demonstrating the existence of an abdominal mass but as a means of determining the effectiveness of the treatment.

The location of metastases is an important consideration from the standpoint of x-ray therapy. In seventeen patients metastases developed in the juxta-aortic nodes on the side of the affected testis. In one patient, the node was on the opposite side; in one patient, nodes on both sides were affected. In two patients metastatis masses developed in the iliac region on the side of the affected testicle. One patient had involvement of the supraclavicular gland without, so far as is recorded, other metastases; as he was not followed in our clinic but received irradiation elsewhere, this observation is not too reliable. In nine patients metastases developed in other areas in addition to those in the abdomen, four in the lungs,

two in the mediastinum and neck, two in the neck and lungs, one in the mediastinum.

The time at which metastases were first detected is worth noting. In twenty-four patients metastases were discovered, in eleven at the time of operation, six within six months after operation, three between six and twelve months after, one between one and two years after, two between two and three years after, one between four and five years after. In short, in 87 per cent of the patients metastases developed within two years after orchidectomy. These figures are of only relative value, since the preoperative duration of the testicular tumor is an unknown factor. It is obvious that the metastases had existed before the testis was removed; those which were not detected until some time afterwards denote either a slow rate of growth or incomplete or faulty observation.

As to those alleged signs of high malignancy, gynecomastia and a positive prolan test, our observations do not prove their value as prognostic indications. Five patients were found to have some degree of gynecomastia. Of these, three survived and two succumbed to the disease.

Fifteen patients had a positive prolan test. The tests varied from six mouse units to 2,000 mouse units (in a man with chorionepithelioma). Eight survived, six died of cancer, and one died of cerebral hemorrhage six months after orchidectomy.

Fourteen had negative prolan tests. Of these, nine survived, five died. The ratio of eight living to six dead of the positive group differs by only 8 per cent from the ratio of nine to five in the negative group.

It is impossible to learn from this series the minimum dosage of x-ray which is effective. In the earlier cases, the dosage was estimated by the "erythema dose." Different types of x-ray apparatus were used, varying from the 200 Kv. to the 100 Kv. machine. A number of the patients were inadequately treated; in a few, treatment was confined to the pelvic region. In several patients, metastatic masses developed just above the limit of irradiation. Within the past eight years, treatment has been much more intelligently planned. It is our belief that at least 1600 r should be given to the anterior abdomen and the same amount to the posterior abdomen, the entire abdomen being included in one field. Chorionepithelioma is so universally fatal that irradiation is useless.

One of the most successful cases was a man who at the time of operation, March, 1935, had a mass opposite the umbilicus. With the 200 Kv. machine he was given 1800 r to the anterior and to the posterior pelvis, and 1500 r to the anterior and posterior upper abdomen. In December, 1935, chest radiographs showed a widening of the mediastinum. He was given 3000 r to this area. He is alive and well today, eight years after his first treatment.

TABLE II.—DURATION OF SYMPTOMS

Under 1 month	5
1 to 3 months	7
3 to 6 months	10
6 to 9 months	2
9 to 12 months	6
About 2 years	4
About 6 years	1
Not stated	15
	50

A recent case may be quoted as an example of modern x-ray therapy. The left testicle had been enlarged for six months. Radiographs of the chest and skull showed no metastases. An intravenous pyelogram was normal. Orchidectomy was done; the testis was the seat of an embryonal carcinoma. One month after operation he was treated with the 1000 Kv. machine at 140 cm. tube to skin distance. In twenty-four treatments he was given 1575 r over the anterior abdomen, the entire abdomen being included in the field, and 1500 r over the posterior abdomen

As a rule, we do not irradiate the chest unless metastases are demonstrable, but from a study of these fifty patients it is our impression that all patients with known abdominal metastases should have treatment to the mediastinum as well. Our figures show that 50 per cent of the patients with metastases in the upper abdomen developed metastases in the chest.

A few statistics gathered from this series of fifty patients are shown in Tables I and II. The fourth decade yielded the most cases; 34 per cent occurred during this period. Right and left testes were equally susceptible.

The duration of testicular enlargement does not appear particularly significant (Table II). The intelligence of the patient and his reaction to the existence of physical abnormalities are indeterminable factors. In a few instances the tumor developed within a

hydrocele which had existed for years. It was noted that the proportion of those who succumbed to those who survived increased with the duration of the tumor, although two who were cured had noticed testicular enlargement for three years in one case and for seven years in another.

TABLE III.—RESULTS

1.	No metastases, no x-ray treatment	8
	Living and apparently well	4
	Years: 1, 2½, 9, 9½	
	Living but with recurrences	2
	Years: 1, 2½	
	Died of disease	2
	Years: 12, 3	
2.	No x-ray treatment until metastases developed	5
	Died: Under 1 year, 4. 3½ years, 1.	
3.	Metastases at time of operation, x-ray treatment	7
	Living and apparently well: 3.	
	Elapsed time: 2, 2½, 8 years.	
	Died: Under 1 year, 3. 2½ years, 1.	
4.	Metastases at time of operation, no x-ray treatment	3
	Died: Under 1 year, 3.	
5.	Miscellaneous.	
	No operation, no x-ray treatment. Died 2 weeks	1
	No operation, x-ray treatment. Died 6 months	1
6.	No metastases, x-ray treatment	23
	Died of cancer	4
	Duration of life: 1, 3, 3½, 11 years	
	Alive without recurrence	19
	Time since operation:	
	1 year or less	2
	1-2 years	2
	2-3 years	2
	4-5 years	1
	5-6 years	5
	6-7 years	2
	7½, 9, 10, 13, 14 years—one each	5
		19

The results of treatment are given in Table III. In view of the fact that when metastases developed, they were noted within two years after orchectomy in 87 per cent, we are justified in assuming that nine out of ten patients who showed no metastases after two years had a good chance of being cured.

CONCLUSIONS

Fifty cases of malignant tumor of the testicle are reviewed. These include two chorionepitheliomas and two cases of bilateral tumor.

Approximately twice as many cases occurred in the fourth decade as occurred in any other decade.

Gynecomastia and positive prolan tests proved to have little prognostic value.

In the patients who developed metastases, these metastases were discovered within two years after orchidectomy in 87 per cent.

Of eight patients without metastases not treated by x-ray, two have lived over four years.

Of twenty-three patients without metastases treated by x-ray, thirteen were in good health four or more years after operation.

Many of the poor results followed incomplete irradiation of the abdomen, as metastases developed in areas that had not been treated.

The ultimate results of x-ray treatment which had been postponed until metastases had developed were not good.

Of twelve patients with metastases, three responded well to irradiation. One of these has lived over four years, two between two and three years.

In patients in whom metastases have developed, the chest as well as the abdomen should be irradiated.

The value of x-ray treatment is proved by the results obtained in this series of cases.

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ACID AND ALKALINE PHOSPHATASE DETERMINATIONS IN PROSTATIC CARCINOMA: BONE AND SOFT PART METASTASES

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In 1938 the present authors made a preliminary report of studies of acid phosphatase in the serum of patients with carcinoma of the prostate.[1] Since that time we have modified our experimental procedure somewhat,[6] using determinations of the acid and alkaline phosphatases in the serum in the diagnosis of metastasizing carcinoma of the prostate, and in following the course of cases of this disease during treatment.[2] During the same period, numerous reports of investigations of serum acid phosphatase in prostatic disease have been made from other institutions.[3,4,5] In general the results obtained by independent students, often working with different methods, have been remarkably consistent. Our findings are summarized below.

Many tissues contain enzymes which split organic phosporus compounds to give free phosphoric acid. The phosphatases from different sources differ in the pH at which they are most active. Those which are most active in acid solution are known as acid phosphatases: those most active in alkaline solution are alkaline phosphatases. Several organs, such as liver, kidney, ovary, testis, et cetera, and most carcinomas and lymphomatoid tumors contain small amounts of acid phosphatase and even smaller amounts of alkaline phosphatase. Normal resting adult bone contains a little alkaline phosphatase, but when bone is growing or responding to injury its alkaline phosphatase increases enormously, sometimes reaching several hundred times the resting level. There is not a rise in the acid phosphatase of bone corresponding to this rise in the alkaline phosphatase. The prostate gland, whether normal, hypertrophied, or cancerous, contains very large amounts of acid phosphatase, the activity per gram reaching a thousand times that of any other tissue. There is no alkaline phosphatase in prostatic tissue itself, although there may be small amounts in the endothelial cells of the vessels in the gland.

Normal blood serum contains small amounts of acid phosphatase and larger amounts of alkaline phosphatase. The ratio of acid to alkaline phosphatase in the serum is normally one to ten when both are measured by their action on beta glycerophosphate. The source of acid phosphatase in normal serum is unknown, but it is obviously not the prostate, since the serum acid phosphatase of normal men and women is the same. Nearly all the alkaline phosphatase of the serum comes from the bones. Bone phosphatase apparently enters the circulation very readily, and serum alkaline phosphatase is usually a sensitive indicator of bone activity. The alkaline phosphatase of the serum is excreted by the liver, and, when liver function is impaired, the serum alkaline phosphatase may rise. The high serum values in hepatic dysfunction should not be confused with those due to bone disease. Serum acid phosphatase is not affected by the liver.

As explained above, the acid phosphatase from the normal prostate does not enter the circulation in appreciable amounts. This is also true of the cancerous prostate as long as the capsule is intact. As soon as a cancer of the prostate begins to spread by local infiltration or distant metastases, whether to soft parts or to bone, the acid phosphatase of the serum may, and usually does, rise. In a series of fifty-seven cases of carcinoma of the prostate which were considered inoperable because of local extension or distant metastases, thirty-eight (67 per cent) had a definite elevation of the serum acid phosphatase; four (7 per cent) had a borderline elevation; and fifteen (26 per cent) had normal readings. In a few of the last group the evidence of local extension was slight, and it is possible that the capsule was still intact, but in the majority of this group there was unquestionable evidence of metastatic disease, and in some the metastases were extensive. It appears, then, that there are some metastases from carcinoma of the prostate which do not discharge acid phosphatase into the blood stream. We have not yet sufficient autopsy material to determine whether this is due to deficiency of the enzyme in the tumor or to some peculiarity in the tumor blood supply. While normal values for the serum acid phosphatase do not exclude the presence of metastasizing carcinoma of the prostate, a definite elevation in the serum acid phosphatase is generally considered pathognomonic of this condition.

Determinations of the serum acid phosphatase give a good indi-

cation of the effectiveness of therapy. After orchidectomy there is usually a sudden drop in serum acid phosphatase to levels within, or slightly above, the normal range.* The drop is ordinarily apparent within forty-eight hours after operation and may be complete within the week, although in some patients there is a slower decrease over a period of a month. The change is often striking, amounting in one of our patients to a fall from 103 units to 2 units per 100 c.c. of serum. In our experience patients whose acid phosphatase fails to drop promptly after orchidectomy show little clinical benefit from the procedure, and usually pursue a steady downward course. Changes in acid phosphatase following the institution of stilbesterol therapy are similar to those after orchidectomy, but appear somewhat more slowly. If patients who have shown clinical improvement and acid phosphatase drop with endocrine therapy later relapse, the clinical relapse is usually preceded or accompanied by a rise in acid phosphatase.

An increase in the alkaline phosphatase of the serum is not pathognomonic of any one type of bone disease. It is a non-specific response to bone injury, and indicates bone growth or an attempt at bone repair. It occurs in osteogenic sarcoma and osteitis deformans, where abnormal new bone is being formed. It occurs in rickets, osteomalacia, hyperthyroidism and some types of inflammatory bone disease, in all of which an attempt at healing is being made. When cancer of soft part origin metastasizes to bone, an attempt at repair may or may not be made. The reason for the difference in the response of the bone to invasion by various types of tumors is not known. It is, of course, a well-established clinical observation that metastases from breast and thyroid cancers, for instance, are usually osteolytic, while those from cancers of the prostate are nearly always osteoplastic. In patients with osteolytic bone metastases the serum alkaline phosphatase is normal or slightly raised, while in patients with osteoplastic metastases it is often very high. The majority of our patients with prostatic cancer had bone metastases when first seen. In four of these the process was predominantly destructive and the serum alkaline phosphatase was normal. In the remaining thirty-eight cases, the metastases were of the usual productive type, and the serum alkaline phosphatase was

*The normal limits of serum acid phosphatase are 0 to 0.9 units; serum alkaline phosphatase 1.5 to 5 units.

high. The patients without bone metastases had normal alkaline phosphatase values which did not change during treatment.

Since the increase in serum alkaline phosphatase in these patients represents a response to bone injury, one would expect that, when the injurious agent (the metastatic carcinoma) is inactivated by endocrine treatment, the alkaline phosphatase would begin to fall. The fall might be expected to be slow, since excess alkaline phosphatase would be required as long as bone repair continued. If, after several months, bone repair is nearly complete, the alkaline phosphatase of the serum should reach normal. The changes in alkaline serum phosphatase actually observed have been, in general, different from those expected. Of the patients with initial high alkaline phosphatase values who had orchidectomies, 67 per cent showed a further rise in alkaline phosphatase within one month after operation. A similar rise was also observed in patients treated with stilbestrol, but only one-third as often as after surgical castration. In most patients in whom the alkaline phosphatase rose after the institution of treatment, it remained high for only two to three months, and then fell to, or below, the initial level. In most patients the degree of osteoplasia of the metastases increased following endocrine treatment, but in some this appeared to indicate healing, while in others the metastatic areas became larger and more numerous. The latter change occurred even in several patients who were entirely relieved of pain and other symptoms referable to the bones. In general, there was no close correlation between the changes in alkaline serum phosphatase and the clinical or roentgenographic status of the patient. There is at present no adequate explanation of the rise in serum alkaline phosphatase which so frequently follows the institution of endocrine therapy.

In summary, treatment of patients with carcinoma of the prostate by orchidectomy or stilbestrol causes a drop in the serum acid phosphatase which indicates a profound inhibition in the enzyme activity of the tumor. The treatment causes changes in the alkaline phosphatase which cannot be explained adequately at present, but which open important fields for future investigation of metastatic processes in bone.

The following histories illustrate the behavior of the acid and alkaline phosphatase in various classes of cases.

Case 1.—B. entered Memorial Hospital in July, 1941, with a large

fixed prostatic carcinoma extending beyond the prostate. He had extensive bone metastases in the pelvis and spine. His serum acid phosphatase varied between 27 and 36 units in July and September, 1941. His serum alkaline phosphatase fluctuated between 26 and 66 units from July, 1941, to March, 1942. He was given stilbesterol 5 mg. daily from September, 1941. This had little effect upon his serum alkaline phosphatase but caused a drop in his serum acid phosphatase to 4 units in March, 1942.

Case 2.—S. entered the Memorial Hospital in January, 1939, with a tumor of the ischium extending into the soft parts. His serum alkaline phosphatase was 6.0 units (slightly higher than normal) and his serum acid phosphatase 0.6 (normal). Aspiration of the tumor revealed a metastatic carcinoma. Treatment of the tumor of the ischium with mild x-ray therapy had no effect upon the phosphatase. Later, the serum acid phosphatase rose above normal and an aspiration biopsy of the prostate showed carcinoma. Then treatment of the entire pelvis by deep x-ray therapy caused a drop in the alkaline and acid phosphatase to normal. Later there was a relapse when the serum acid phosphatase inceased faster than the serum alkaline phosphatase. This showed that the effect of the deep x-ray therapy was greater upon the bone metastasis than upon the prostate.

Case 3.—S. entered the Memorial Hospital in June, 1941, with an extensive fixed prostatic carcinoma with metastasis to his spine. His serum acid phosphatase varied between 34 and 76 units. His serum alkaline phosphatase was from 6.5 to 9.5. X-ray castration (1500R) had but slight effect upon either his acid or alkaline phosphatase. Later he was given stilbesterol 5 mg. daily. This reduced his acid phosphatase to 1.0 unit.

Case 4.—L. came to the Memorial Hospital with a tumor of the tibia. His serum alkaline phosphatase was 14 units and his serum acid phosphatase 5 units. Examination of his prostate showed an extensive fixed prostatic carcinoma. Irradiation of the tibial tumor caused a recession of the tumor to nearly normal. Both his serum alkaline and acid phosphatase decreased but not to normal. He later had an orchidectomy which resulted in a reduction in his serum alkaline phosphatase to 6.6 and his serum acid phosphatase to 0.8—both very nearly normal.

Case 5.—M. came to the Memorial Hospital with a mass in his lung consistant with primary lung carcinoma. His serum alkaline phosphatase was 12 units and his serum acid phosphatase 11. This indicated the prostate as a source of the carcinoma. Aspiration of the prostate showed carcinoma. Aspiration of the lung showed adeno-carcinoma, consistent with primary prostatic carcinoma. He then was given stilbestrol medication. His serum acid phosphatase went to normal. His serum alkaline phosphatase increased and then came down to normal. There was a clinical improvement and the mass in the lung regressed.

Now he is symptom-free, with some regression of the mass in his prostate.

We have had two cases of bladder carcinoma with bone metastases, with quite contradictory readings of the serum alkaline phosphatase. The first patient had a Grade III bladder carcinoma with alterations in the right ilium and upper femur suggesting metastases. His serum alkaline phosphatase varied between 28.9 and 36.6 units. The acid phosphatase was normal. At autopsy a metastatic lesion of the femur, partly osteoplastic and partly osteolytic, was found. The second patient had an extensive Grade III bladder carcinoma. The prostate was small, regular, soft and there was no residual urine. Roentgenogram showed extensive osteoplastic metastases of the pelvis, lumbar spine, and skull. His acid phosphatase varied between 0.08 and 0.17 units and his alkaline phosphatase between 5.6 and 4.4 units. At the present time, eight months after his cystotomy operation, both his bladder lesion and his bone metastases are quiescent. Further study will have to explain such variations.

The bladder tumor in the first case was extremely malignant; in the second, it was much less so. It is possible that the much higher serum alkaline phosphatase in the first case represented an intense defensive reaction on the part of the bone against a very aggressive metastatic process. In the second case, where the tumor was less active, a less intense bone defense may have sufficed to hold the invasion partly in check by new formation.

We have had a case of what was an extensive lymphosarcoma of the prostate with large metastases to the left inguinal glands, with a serum acid phosphatase of 0.18 units and an alkaline phosphatase of 5.6 units. The patient came to the Memorial Hospital with a massive tumor of the left inguinal region and an edematous and almost useless left leg. Aspiration of an extensive prostatic and periprostatic tumor showed what Dr. Stewart believed to be a lymphosarcoma of the prostate. Radiation of the inguinal mass caused a rapid regression of the tumor which seemed to confirm the diagnosis of lymphosarcoma.

The explanation of the normal serum acid phosphatase readings is that lymphoid tissue, as contrasted with prostatic tissue, contains little acid phosphatase.

SUMMARY

The serum acid phosphatase of two-thirds of our patients with

metastasizing carcinoma of the prostate was elevated when the patients were first examined.

The serum alkaline phosphatase of all patients with osteoplastic metastases from carcinoma of the prostate was markedly elevated. In a few prostatic cases the metastases were osteolytic. In these the serum alkaline phosphatase was normal or very slightly elevated.

In patients whose serum acid phosphatase was initially elevated, and who showed a satisfactory clinical response to treatment by stilbestrol or surgical castration, the acid phosphatase fell promptly nearly to normal. Patients whose acid phosphatase failed to show a conspicuous drop within two weeks after the institution of endocrine treatment likewise failed to show clinical improvement.

In patients whose serum alkaline phosphatase was initially elevated, two-thirds showed a further rise after surgical castration and one-fourth after the institution of stilbestrol therapy. This rise was usually accompanied by an increase in the degree of osteoplasia of the bone metastases. It was not closely related to clinical response.

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DISCUSSION

DR. BENJAMIN S. BARRINGER (New York, N. Y.): I told Dr. Rathbun I wouldn't ask to close if I could just thank Dr. Smith for his paper and touch on one point.

I published the autopsy results of some thirty-five cases of teratoma testis. Those results are very amazing to me. They taught me things I never knew before of teratoma testis. Among other results, in practically 100 per cent of the cases that died, there was a bilateral abdominal invasion, either of the spleen or kidney or retroperineal gland or the glands that had crossed over. In a large percentage of cases there were renal or perirenal invasions by the tumor. In 75 per cent of all cases that had lung invasion, the liver was involved.

That brings me down to the point, how can one ever cure a case of teratoma testis after the teratoma has gone beyond the testis? If you carried this to the last degree, you would x-ray the entire body from head to heels, and, therefore, I would object to Dr. Smith's x-raying the lung before there were visible metastases in the lungs. I think you have got to be reasonable and wait in some cases until things happen.

DR. WILLIAM P. HERBST, JR. (Washington, D. C.): I would like to ask Dr. Smith whether he had contemplated removing the sound testicle in any of the cases after metastasis had formed, following out the observations that Dr. McClelland reported last year. I have been looking for a case that had demonstrable metastasis after castration to do that on and try it, but so far I haven't had one.

DR. SMITH: I didn't quite understand. Cases that had no metastases at the time of operation who developed them later, is that what you mean?

DR. HERBST: Yes, after they develop them later, would you contemplate or consider it advisable to try removing the sound testicle after you removed the original one, as a form of treatment in controlling the metastatic process? Dr. McClelland last year reported some very interesting observations on two cases.

Dr. Barringer, I would like to ask you what you think about a

report in the literature not so long ago by an Englishman of a young woman, I think eighteen years of age, who had a malignancy, a sarcoma of the right femur, which did not respond to extensive x-ray therapy. The leg was amputated. Subsequently, an inguinal metastatic lesion developed which they intended to treat with radium, but which they didn't do on account of hemorrhage. This fellow gave first 5 and then 10 and I think eventually 15 milligrams of stilbestrol a day in conjunction with x-ray treatment and eventually controlled the metastatic lesion at the time he reported it.

I just wondered whether you had any explanation of that in a woman.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): Did I understand that the alkaline phosphatase was increased in parathyroid disease? Is that correct?

DR. BARRINGER: Yes.

DR. LIVERMORE: If that is correct, then wouldn't it be a good idea for us to test for alkaline phosphatase in cases of recurrent stone where we suspect parathyroid disease?

DR. BARRINGER: I think it might.

DR. J. C. MCCLELLAND (Toronto, Canada): I mentioned a case last year that was referred to by Dr. Herbst. I think it might be interesting for you to know the subsequent history of that now. Some of you may recall the patient was in the Royal Norwegian Air Force, and he had had an orchectomy on the 15th of October, 1941. At that time, this man was just about dead. He had secondary lesions in both his abdomen and his lungs, and it was a question at the time whether he would recover from the operation. The remaining testicle was removed, and he proceeded to get better. He went up North and he skied all that winter, and early in the spring of 1942 he went back to duty. He carried on his duties through the summer, when an x-ray of his chest showed secondary lesions again, although a previous x-ray had shown the chest apparently clear. In the summer, he began to go downhill and he gradually went down with more secondary lesions. He had more x-ray treatment—a tremendous amount. I can't say whether he had 1600 r or not, Dr. Smith, but he did have a good deal of radiation. He died in January of this year.

Now, something happened from October 15, 1941, that improved him, and then he went down and died this past January, 1943. An autopsy was held, and he had secondary lesions throughout the abdomen and also secondary lesions in the lungs.

DR. NESBIT: When was his first x-ray therapy?

DR. MCCLELLAND: His first x-ray therapy was previous to the orchectomy. His original orchectomy, I think, was in February, 1941.

DR. GEORGE G. SMITH (Boston, Mass.): In regard to Hinman's operation, I personally have never done it, because the metastases of the radiosensitive type of testicular tumor can be controlled by x-ray, and in a considerable proportion of those cases the lungs are involved early in the course of the disease. I felt unable to differentiate the cases which would be non-radiosensitive.

I believe there is a small group of patients for whom this radical operation may be of value. Those are certain teratomas but there, again, the metastasis from a teratoma which in itself is largely resistant to irradiation, may be radiosensitive. Hinman himself says there is no use in doing the operation when the metastases are palpable, so that cuts out a large proportion of these cases. It seemed, therefore, that the cases suitable for this operation were so few in number that they were very difficult to identify.

In regard to pre-operative x-ray, we haven't done it because, in the first place, I can see no reason why the operation of cutting down on the spermatic cord and immediately ligating it before the testicle is touched at all is going to spread metastases. The distinct disadvantage of pre-operative irradiation is that you may entirely upset the pathological report on the tumor which is removed.

Another thing is, some of these testicular tumors are not what you think they are, and to give a patient an adequate course of irradiation which is quite a thing for him and then to find that he has a fibroma or leiomyofibroma or something like that, is disconcerting to say the least.

Now, in regard to the cure of pulmonary cases that Dr. Barringer speaks of, one of the patients in this series was a man who in 1935 had a castration for embryonal carcinoma of the left testicle. At the same time it seemed that he had a resistance to the left of his umbilicus. He was a stout fellow, and it was a little difficult to be

sure. We treated his entire abdomen, and this mass has never appeared since then. That was in May, 1935. In December, 1935, he showed a gland in the neck and evidence of widening of the mediastinum. He was given 3000 r to the chest through two fields, anterior and posterior. His mediastinum shrunk down to normal. He is the chief plumber at the Massachusetts General Hospital and we have seen him regularly every three months. He has been x-rayed frequently. His health is perfect and he has never shown any evidence of further recurrence of his tumor.

Dr. Herbst asked about removal of the remaining testicle. I haven't done that because I can see no logic in it. Dr. Jenkins reported some patients on whom he had done that, but both his patients had had deep x-ray therapy. He said that the glands were still there two months afterward, but that doesn't necessarily mean that the x-ray therapy was not effective, because it may take longer than that to get the full result. The same thing is true in Dr. McClelland's patient. He had had some x-ray therapy, and I maintain that unless you can demonstrate improvement following orchidectomy on the sound side, in a patient who has had no x-ray therapy at all, you can't be at all sure that orchidectomy has been the beneficial factor.

DR. BARRINGER: I think Dr. Smith misunderstood me. You believe in x-ray therapy after the lesion has been established in the chest, certainly, which was the case in this patient you just cited, wasn't it?

DR. SMITH: Yes, but you asked if there was any patient who had ever been cured who showed metastases in the lungs.

DR. BARRINGER: Only in a vague way. I said it was a wonder to me that the patient who had metastasis in the lung was ever cured. We have them cured; we all know that.

As far as Dr. Herbst's question goes, I do not know the answer.